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6-5-3FSUM 10551.1  
PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Robert A. Holton et al.

ART UNIT 1625

Serial No. 09/978,436

Filed October 16, 2001

Confirmation No. 5339

For RADIOSENSITIZING TAXANES AND THEIR PHARMACEUTICAL PREPARATIONS

DECLARATION OF PRIOR INVENTION UNDER 37 C.F.R. ' 1.131

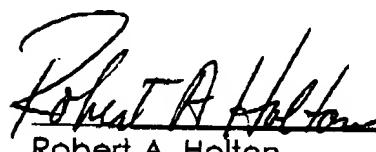
We, Robert A. Holton, Hossain Nadizadeh and Li-Xi Yang declare as follows:

1. We are the inventors of the subject matter claimed in the above-entitled United States patent application.
2. We are submitting this Declaration to establish completion of our invention in the U.S. before June 7, 1995, the filing date of U.S. Patent No. 5,780,653.
3. We reduced to practice the invention claimed in this application in the United States before June 7, 1995.
4. Facts in support of this Declaration are attached hereto as Exhibit A. Exhibit A is a true and correct copy of experimental note book page numbers 1-6, 8-14, 16, 18, 20, 22-28, 30-38, 40, 42-44, 46, 48, 50, 52, 54-62, 64, 66, 68-74, 76-78, pages 1-4 of "Taxol and TM 24 hrs prior Xray," pages 1-3 of "TM drug,"

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PATENT

pages 1-3 of 'TNB,' 'TNB+22Gy' and 'TNB control' (with dates deleted), upon which Figures 1-18 and Examples 4.1, 4.2, 4.4, 4.5, 4.6 of this application are based. Specifically, compound taxol-metro (or TM) corresponds to N-debenzoyl-N-(t-butylcarbamoyl)-7-(metronidazoleoxycarbonyl)taxol of Example 2 and nitrophenyl taxol (or taxol nitrobenzene or TNB) corresponds to N-debenzoyl-N-(t-butylcarbamoyl)-3'-desphenyl-3'-(4-nitrophenyl)taxol of Example 3 of this application. As such, Exhibit A evidences our reduction to practice of the invention claimed in the application prior to June 7, 1995.

5. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. ' 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

  
\_\_\_\_\_  
Robert A. Holton  
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Date

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Hossain Nadizadeh

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Date

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Li-Xi Yang

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Date

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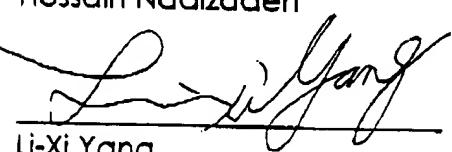
Robert A. Holton

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Date

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Hossain Nadizadeh



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Li-Xi Yang

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Date

4/28/03

Date

FSUM 10551.1  
PATENT

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Robert A. Holton

Date

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Nadizadeh

Hossain Nadizadeh

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4/28/03

Date

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Li-Xi Yang

Date

~~metronidazole - CL and metronidazole - I~~ Toxicity under  $O_2 / N_2$

$358/8 = 4.4 \times 10^5$ ,  $1 + 2L = 2 \times 10^2$ ,  $0.1 + 2.1 = 2 \times 10^0$ ,  $1 + 9 = 2000$ .

$2.5 + 40.5 = 200$ . Each dish: 1 ml drug solution + 2 ml HSS.

200 cells/dish incubated 1h at 37°C

Drugs: solvent: DMSO. 15ul drug solution was added into 2 ml HSS

metro-CL stock: 1.: 1.06M 2.: 0.638M 3.: 0.1276M

metro-I stock: 1.: 0.471M 2.: 0.0952M 3.: 0.01900M

| Gr. nos  | Final Conc (mM) | N <sub>2</sub> colonies | O <sub>2</sub> colonies     | mean                | SF     | SF/PE |
|----------|-----------------|-------------------------|-----------------------------|---------------------|--------|-------|
| 0        | 0               | 135                     | 126, 162, 151, 0.147, 0.73  | 135                 | 0.68   |       |
| metro-I  | 1. 3.54         | 15, 0, 3                | 124, 115, 125, 0.131, 0.61  | 16.73, 0.037        | 0.054  |       |
| 2        | 0.71            | 22,                     | 150, 129, 153, 0.144, 0.73  | 16.22, 0.111, 0.162 | 0.831  |       |
| 3        | 0.14            | 28, 45, 46              | 87 117 138, 0.144, 0.57     | 39.7, 0.198         | 0.392  |       |
| metro-CL | 1. 7.89         | 41, 35                  | 116, 103 110, 0.146, 0.58   | 38, 0.191           | 0.379  |       |
| 2.       | 4.75            | 99                      | 152, 151, 159, 0.154, 0.77  | 99, 0.495           | 0.728, |       |
| 3.       | 0.95            | 130, 156, 124,          | 156, 151, 147, 0.153, 0.757 | 136.7, 0.683        | 1.00   |       |
|          |                 |                         |                             |                     |        | 1.04  |

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Cytotoxicity for metra-Cl, metra-I, metra-CHO under N<sub>2</sub>/O<sub>2</sub>.

Drugs: metra-Cl and metra-I were prepared on 1/24.

metra-CHO: 2.655M stock:

$$\text{dilutions: } 1. 19.8 \text{ ml stock} + 26 \text{ ml HSS} = 46.76 \text{ mM}$$

$$2. 97.5 \text{ ml stock} + 26 \text{ ml HSS} = 9.919 \text{ mM}$$

Each dish plated 200 cells. 3. 48.75 ml stock + 26 ml HSS = 4.97 mM.

N<sub>2</sub> Colonies in Dish O<sub>2</sub> Colonies in Dish

M-CHO 1. 0 0

M-CHO 2. 0 0

M-CHO 3. 0 0

|  | N <sub>2</sub> Count | mean | SF | SF/PE | O <sub>2</sub> Count | mean | SF | SF/PE |
|--|----------------------|------|----|-------|----------------------|------|----|-------|
|--|----------------------|------|----|-------|----------------------|------|----|-------|

|        |                |       |      |      |                |       |      |      |
|--------|----------------|-------|------|------|----------------|-------|------|------|
| -Cl 3. | 128, 109, 119. | 118.7 | 0.59 | 0.91 | 156, 136, 159. | 150.3 | 0.75 | 1.00 |
|--------|----------------|-------|------|------|----------------|-------|------|------|

|        |                |       |      |      |               |       |      |      |
|--------|----------------|-------|------|------|---------------|-------|------|------|
| M-Cl 2 | 122, 112, 121. | 118.3 | 0.59 | 0.91 | 142, 140, 130 | 137.3 | 0.69 | 0.92 |
|--------|----------------|-------|------|------|---------------|-------|------|------|

|        |             |    |      |      |                   |       |      |      |
|--------|-------------|----|------|------|-------------------|-------|------|------|
| M-C 3. | 100, 86, 90 | 92 | 0.46 | 0.71 | 107, 85, 125, 117 | 116.3 | 0.58 | 0.78 |
|--------|-------------|----|------|------|-------------------|-------|------|------|

|        |               |       |      |      |               |      |      |      |
|--------|---------------|-------|------|------|---------------|------|------|------|
| M-I 3. | 133, 145, 134 | 137.3 | 0.69 | 1.06 | 136, 132, 140 | 136. | 0.68 | 0.91 |
|--------|---------------|-------|------|------|---------------|------|------|------|

|        |               |       |      |      |               |       |      |      |
|--------|---------------|-------|------|------|---------------|-------|------|------|
| M-I 2. | 101, 103, 101 | 101.7 | 0.51 | 0.78 | 146, 156, 128 | 143.3 | 0.72 | 0.96 |
|--------|---------------|-------|------|------|---------------|-------|------|------|

|        |              |      |      |      |               |       |      |      |
|--------|--------------|------|------|------|---------------|-------|------|------|
| M-I 1. | 65, 101, 103 | 99.7 | 0.50 | 0.77 | 156, 136, 159 | 150.3 | 0.75 | 1.00 |
|--------|--------------|------|------|------|---------------|-------|------|------|

|    |               |       |      |      |      |          |     |      |
|----|---------------|-------|------|------|------|----------|-----|------|
| O. | 131, 127, 130 | 129.3 | 0.65 | (PE) | 159. | 152, 139 | 150 | 0.75 |
|----|---------------|-------|------|------|------|----------|-----|------|

Cysteine of  $(\text{ceto})_2\text{N}(\text{CH}_2)_3\text{N}(\text{ceto})_2$ :

Drop:  $0.3772/1.3 \text{ ml. } d = 1.1772/\text{ml.} = 1.03 \text{ ml. stock.}$

Working dilutions: 1.:  $135 \text{ ml.} + 19 \text{ ml. H2O} = 12.91 \text{ ml.}$

2.:  $67.5 \text{ ml.} + 19 \text{ ml. H2O} = 6.48 \text{ ml.}$

3.:  $33.75 \text{ ml.} + 19 \text{ ml. H2O} = 3.24 \text{ ml.}$

Results:  $\text{N}_2 \quad \text{O}_2$

Calories 0 129, 109, 126. 135, 113, 110

|    |   |   |   |   |   |   |
|----|---|---|---|---|---|---|
| 1. | 0 | 0 | 0 | 0 | 0 | 0 |
|----|---|---|---|---|---|---|

|    |   |   |   |
|----|---|---|---|
| 2. | 0 | 0 | 0 |
|----|---|---|---|

|    |         |   |
|----|---------|---|
| 3. | 2.5. 5. | 0 |
|----|---------|---|

1. Radiosensitization of metronidazole-Cl at 7.82 mM

| Radiation dose (minutes) | Hyper + Drug cells | Hyper cells | Direct Drug cells | Oxic cells |
|--------------------------|--------------------|-------------|-------------------|------------|
| 20 Gy (10')              | 20,000             | 10,000      |                   |            |
| 12 Gy (6')               | 2000               | 1,000       |                   |            |
| 6 Gy (3')                | 1,000              | 500         |                   |            |
| 0                        | 200                | 200         |                   |            |
| 8 Gy (4')                |                    |             | 20,000            | 20,000     |
| 6 Gy (3')                |                    |             | 5,000             | 5,000      |
| 4 Gy (2')                |                    |             | 1,000             | 1,000      |
| 0                        |                    |             | 200               | 200        |

2. Cytotoxicity of metronidazole-aldehyde under O<sub>2</sub> conditions

Each dish contains 200 cells, each group 3 dishes

Final Conc: #1: 0.01 mM. #2: 0.1 mM. #3: 1 mM. treated for 2h.

| Count # | N <sub>2</sub> +Drug | mean | SF     | SF/PE   | N <sub>2</sub> | mean | SF    | SF/PE  |
|---------|----------------------|------|--------|---------|----------------|------|-------|--------|
| 20 Gy   | 2. 2. 2              | 2    | ±.0001 | 0.00027 | 57.6958        | 61.3 | 0.006 | 0.0186 |

|       |          |    |       |        |         |      |        |       |
|-------|----------|----|-------|--------|---------|------|--------|-------|
| 12 Gy | 13. 9. 8 | 10 | ±.005 | 0.0135 | 63.5657 | 58.7 | 0.0587 | 0.159 |
|-------|----------|----|-------|--------|---------|------|--------|-------|

|      |             |    |       |       |             |    |       |      |
|------|-------------|----|-------|-------|-------------|----|-------|------|
| 6 Gy | 183. 46. 57 | 87 | ±.087 | 0.235 | 121. 90. 50 | 87 | 0.174 | 0.49 |
|------|-------------|----|-------|-------|-------------|----|-------|------|

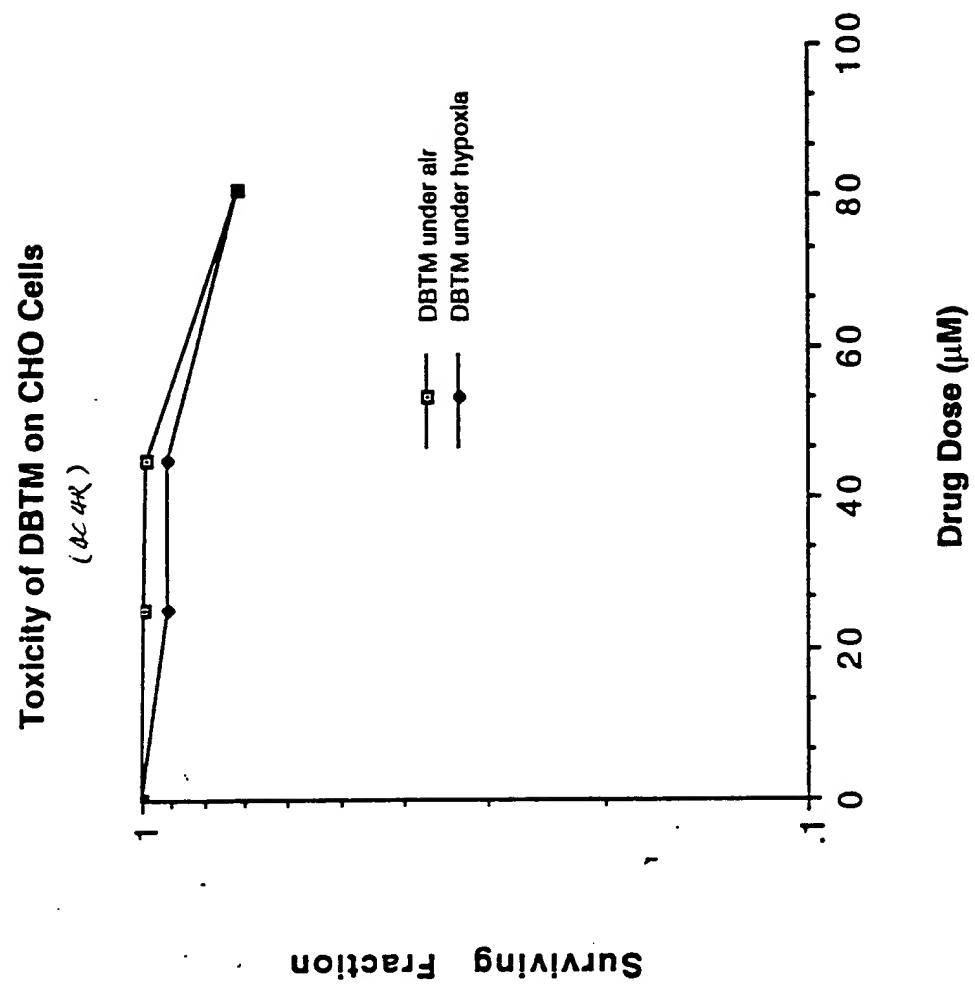
|   |            |      |      |      |              |      |      |  |
|---|------------|------|------|------|--------------|------|------|--|
| 0 | 48. 83. 92 | 74.3 | ±.37 | (PE) | 104. 117. 50 | 90.3 | 0.45 |  |
|---|------------|------|------|------|--------------|------|------|--|

| C <sub>2</sub> +D <sub>1.6</sub> 9 | mean | SF | SF/PE | O <sub>2</sub> | mean | SF | SF/PE |
|------------------------------------|------|----|-------|----------------|------|----|-------|
|------------------------------------|------|----|-------|----------------|------|----|-------|

|      |               |       |      |        |               |      |       |       |
|------|---------------|-------|------|--------|---------------|------|-------|-------|
| 8 Gy | 240. 203. 216 | 289.7 | ±.01 | 0.0297 | 280. 291. 290 | 287. | 0.014 | 0.026 |
|------|---------------|-------|------|--------|---------------|------|-------|-------|

|      |               |       |        |       |               |      |        |       |
|------|---------------|-------|--------|-------|---------------|------|--------|-------|
| 6 Gy | 176. 159. 173 | 169.3 | ±.0339 | 0.045 | 273. 280. 260 | 271. | 0.0542 | 0.099 |
|------|---------------|-------|--------|-------|---------------|------|--------|-------|

|   |            |      |      |      |               |       |      |  |
|---|------------|------|------|------|---------------|-------|------|--|
| 0 | 75. 76. 70 | 73.7 | ±.37 | (PE) | 116. 106. 114 | 110.3 | 0.55 |  |
|---|------------|------|------|------|---------------|-------|------|--|



Cytotoxicity for  $(\text{nitro})_2\text{N}(\text{CH}_2)_3\text{-4N}(\text{nitro})$ , abbreviated to 4C and 3C, under  $\text{N}_2$  or  $\text{O}_2$  conditions. After drug was added into dishes, cells were made hypoxic for 1h at room temperature. Then incubated at  $37^\circ\text{C}$  under hypoxia for another 1h, totaling 2h foroxic cells, treated with drug for 2h in incubator, irradiated at  $19^\circ\text{C}$ ,  $26\text{r/min}$ .

Group: drug  $\text{N}_2/\text{O}_2$  Radiation Dose(Gy) Drug Conc. (mM)

|    |    |              |    |        |
|----|----|--------------|----|--------|
| 1  | 4C | $\text{N}_2$ | 20 | 0.81   |
| 2  | 4C | $\text{N}_2$ | 12 | 0.045  |
| 3  | 4C | $\text{N}_2$ | 6  | 0.0025 |
| 4  | 4C | $\text{O}_2$ | 8  | 0.81   |
| 5  | 4C | $\text{O}_2$ | 6  | 0.045  |
| 6  | 4C | $\text{O}_2$ | 4  | 0.0025 |
| 7  | 3C | $\text{N}_2$ | 20 | 1 mM   |
| 8  | 3C | $\text{N}_2$ | 12 | 0.1    |
| 9  | 3C | $\text{N}_2$ | 6  | 0.01   |
| 10 | 3C | $\text{O}_2$ | 8  | 1-     |
| 11 | 3C | $\text{O}_2$ | 6  | 0.1    |
| 12 | 3C | $\text{O}_2$ | 4  | 0.01   |

| Group | #   | $\text{N}_2$ | mean  | SF    | SF/PE | $\text{O}_2$ | mean  | SF    | SF/PE |
|-------|-----|--------------|-------|-------|-------|--------------|-------|-------|-------|
| 4C    | (1) | 88.91.116    | 48.3  | 0.47  | 0.71  | 98.106.86    | 96.7  | 0.48  | 0.71  |
| 4C    | (2) | 123.120.135  | 126   | 0.63  | 0.91  | 138.127.136  | 133.7 | 0.67  | 0.98  |
| 4C    | (3) | 63.132.142   | 112.3 | 0.56  | 0.81  | 132.138.134  | 134.7 | 0.67  | 0.99  |
| 3C    | (1) | 96.95.131    | 107.3 | 0.54  | 0.78  | 23.35.35     | 31    | 0.155 | 0.23  |
| 3C    | (2) | 56.56.71     | 61    | 0.305 | 0.44  | 106.96.135   | 112.3 | 0.56  | 0.83  |
| 3C    | (3) | 36.61.37     | 44.7  | 0.22  | 0.32  | 94.123.44    | 103.7 | 0.52  | 0.76  |
| C     | (1) | 136.140.139  | 138.3 | 0.67  | (PE)  | 142.126.140  | 136   | 0.68  | (PE)  |

## 1. Radiosensitization of CHO cells by metronidazole-I. (M-I)

Drug M-I: from stocks 4.49M, get 0.5ml, diluted with 0.75ml

DMSO to make a M-I solution of 0.476M, From which

0.54ml was taken, added into 74.56ml HBSS,

giving final conc. of 2.54 mM

Time (min) Radiation (rad)  $N_2 + \text{Drug}$   $O_2$

|    |    |        |        |        |  |
|----|----|--------|--------|--------|--|
| 9. | 18 | 20,000 | 10,000 |        |  |
| 6  | 12 | 2000   | 1000   |        |  |
| 3  | 6  | 1000   | 500    |        |  |
| 0  | 0  | 200    | 200    |        |  |
| 0  | 0  | 2      | 200    | 200    |  |
| 2  | 4  |        | 1000   | 1000   |  |
| 3  | 6  |        | 5000   | 5000   |  |
| 5  | 10 |        | 20000  | 20,000 |  |

Cells were allowed to attach for 2 1/2 h, 3ml of drug was added into

trays dishes, pumped for 1h, or plated in incubator for 1h, then put

in 37°C water bath for 1h, total exposure time to drug was 2h.

irradiated at 48 cm, at 205 rad inside chamber equals 200 rad/min.

Counts  $N_2 + \text{Drug}$  mean SF  $\text{SF/PE}$   $N_2$  mean SF  $\text{SF/PE}$

186sf 0 0 0 0 0 55.75.61 63.7 0.06 0.01

120sf 0 0 0 0 0 58.70.33 53.7 0.056 0.11

66sf 1. 2. 0 1. 0.001 0.056 76. 63. 80 73 0.146 0.29

86sf 3. 7. 1. 3.7 0.018 100. 112. 93 101.7 0.51

$O_2 + \text{Drug}$   $O_2$

106sf 27. 21. 26 24.7 0.04 0.007 74. 89. 78 80.3 0.004 0.005

60sf 95. 97. 67 36.3 0.02 0.049 289. 307. 312 302.7 0.061 0.078

40sf 40. 54. 46 46.7 0.05 0.267 239. 218. 219 225.3 0.225 0.29

0 36. 44. 25 35 0.175 153. 142. 172 155.7 0.78 (PE)

## 2. Taxol and Taxol-mitomycin-cotaxol Toxicity experiments

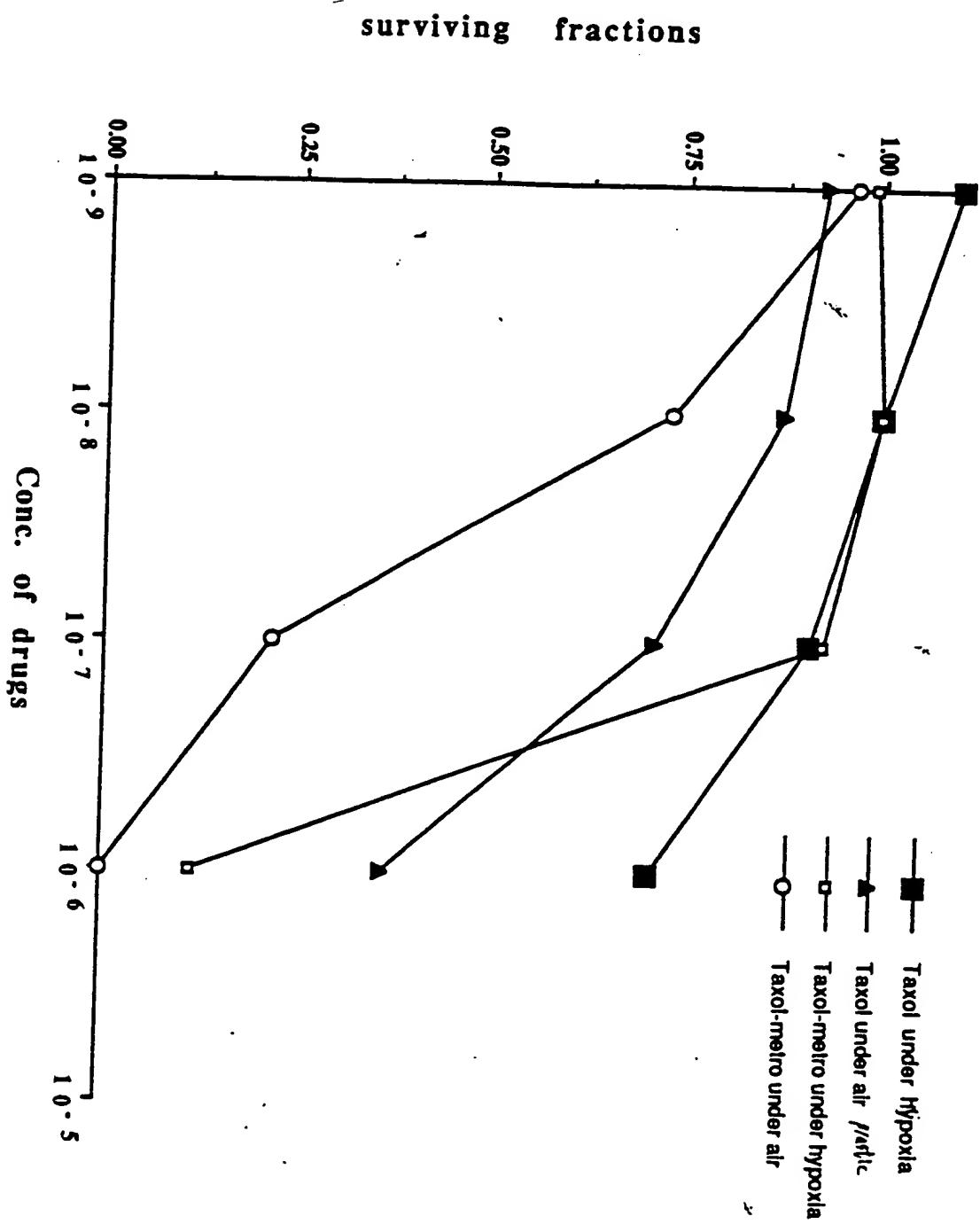
Draft: Taxol:  $8.5 \text{ mg / 1000 units} = 1 \text{ ml N} \xrightarrow{2 \text{ ml + }} 2.475 \text{ ml} \xrightarrow{2 \text{ ml + }} 18 \text{ ml} \xrightarrow{2 \text{ ml + }} 18 \text{ ml} \xrightarrow{2 \text{ ml + }} 18 \text{ ml}$   
 $\xrightarrow{\text{nation}} (15, 20 \text{ ml}) 10^{-5} \xrightarrow{10^{-6}} 10^{-7} \xrightarrow{10^{-7}} 10^{-8} \xrightarrow{10^{-9}} 10^{-9}$

$$\text{Taxol-Metabolism: } \text{Pmg/8.6 \mu M Dose} = 1 \text{ mM} \xrightarrow{\text{2 min}} \text{2.07 mM} \xrightarrow{\text{3 min}} 1.8 \text{ mM} \xrightarrow{\text{10 min}} 1.0 \text{ mM} \xrightarrow{\text{10 min}} 0.8 \text{ mM} \xrightarrow{\text{10 min}} 0.1 \text{ mM}$$

Cells were allowed to attach for 6 h, drugs were added, pumped for 1 h on plates in incubator foroxic group, total drug exposure time was 24 h. Each group had 2 parallel dishes, where 200 cells were plated for each of them.

| each of them |             | Count             | mean  | SF          | SF/PE | $\bar{O}_2$ Count | mean              | SF         | SF/PE  |       |
|--------------|-------------|-------------------|-------|-------------|-------|-------------------|-------------------|------------|--------|-------|
| T-1          | Tarol       | V2                | Count | mean        | SF    | SF/PE             | $\bar{O}_2$ Count | mean       | SF     | SF/PE |
| T-9          | zdish       | 141.157           | 149   | 0.745       | 1.918 | zdish             | 138.145           | 141.5      | 0.7075 | 0.925 |
| T-8          | zdish       | 160.132           | 136   | 0.68        | 1.011 | 128.134           | 133.5             | 0.6875     | 0.873  |       |
| T-7          | zdish       | 131.114.          | 122.5 | 0.6125      | 0.911 | 112.106           | 109               | 0.545      | 0.712  |       |
| T-6          | zdish       | 97. 94.           | 95.5  | 0.4775      | 0.71  | 51. 60            | 55.5              | 0.2775     | 0.363  |       |
| T-0          | zdish       | 132.137.          | 134.5 | 0.6725 (PE) |       | 159.147           | 153               | 0.765 (PE) |        |       |
| Tm-1         | Tarol-petro | $\bar{O}_2$ Count | mean  | SF          | SF/PE | $\bar{O}_2$       |                   |            |        |       |
| Tm-4         | zdish       | 123.143           | 133   | 0.665       | 0.989 | 148.147           | 147.5             | 0.7375     | 0.964  |       |
| Tm-8         |             | 121.150           | 135   | 0.6775      | 1.00  | 112. 111          | 111.5             | 0.5575     | 0.729  |       |
| Tm-7         |             | 122.127           | 124.5 | 0.6225      | 0.926 | 35. 31            | 33                | 0.165      | 0.216  |       |
| Tm-4         |             | 0. 31.            | 15.5  | 0.0775      | 0.05  | 0 0               | 0                 | 0          | 0      |       |

## First Toxicity Experiment for Taxol &amp; Taxol-metro



Radioisotropization of Taxotremat Conc. of  $2 \times 10^{-8} M$

| Time | Radiation (Gy) | $N_2 + \text{Drug}$ | $N_2$  | Time | Radiation (Gy) | $\text{O}_2 + \text{D}$ | $\text{O}_2$ |
|------|----------------|---------------------|--------|------|----------------|-------------------------|--------------|
| 3    | 18             | 20.000              | 10.000 | 4    | 8              | 10.000                  | 10.000       |
| 6    | 12             | 5000                | 2000   | 3    | 6              | 5000                    | 5000         |
| 3    | 6              | 1000                | 500    | 2    | 4              | 1000                    | 1000         |
| 0    | 0              | 200                 | 200    | 0    | 0              | 200                     | 200          |

Drugs from Taxol-metro 1mM  $\rightarrow 0.025 \text{ ml} + 2.075 \text{ ml}$  medium

Plated cell and dish put incubator 6hr then prop 1hr  $1 \text{ ml} + 9 \text{ ml} = 10^{-6}$

with chamber incubator 24 hr. Radiation  $2 \text{ ml} + 18 \text{ ml} = 10^{-7}$

incubator foroxic  $2 \text{ ml} + 8 \text{ ml} = 2 \times 10^{-8}$  Each dish add

| $N_2 + \text{Drug}$ count  | mean        | SF    | S <sup>2</sup> /PE | $N_2$ count        | mean        | SF        | S <sup>2</sup> /PE | 4 ml   |
|----------------------------|-------------|-------|--------------------|--------------------|-------------|-----------|--------------------|--------|
| 180f                       | 66.69.99    | 78    | 0.0034             | 5.006              | 83.32.95    | 86.7      | 0.0087             | 0.011  |
| 126f                       | 36.391.397  | 298   | 0.0535             | 5.094              | 218.200.220 | 212.7     | 0.106              | 0.1399 |
| 66f                        | 272.270.284 | 275.3 | 0.215              | 0.414              | 232.350.248 | 243.3     | 0.487              | 0.64   |
| 0                          | 146.114.123 | 127   | 0.635 (PE)         | 162.146.148        | 152         | 0.76 (PE) |                    | 0      |
| $\text{O}_2 + \text{Drug}$ |             |       |                    | $\text{O}_2$ count |             |           |                    |        |
| 86f                        | 87.14.85    | 97.7  | 0.0398             | 0.022              | 188.149.194 | 193.7     | 0.019              | 0.025  |
| 66f                        | 156.146.147 | 123.3 | 0.03               | 0.067              | 400.38.393  | 396       | 0.079              | 0.104  |
| 46f                        | 148.126.134 | 136   | 0.136              | 0.306              | 333.353.356 | 347.3     | 0.347              | 0.457  |
| 0                          | 88.90.89    | 89    | 5.045 (PE)         | 160.145.151        | 152         | 0.76 (PE) |                    | 0      |

Radiosensitization of T9EL conc of  $10^{-7}$

Drugs - 1:1000 in medium -  $2.5 \text{ ml} + 2.475 \text{ ml} = 10^{-5}$

(medium)

$+ 10^{-6}$

$+ 10^{-7}$

$C_2$

$CO_2$

Radiosensitization of  $(\text{metr})_2\text{N}(\text{CH}_3)_2\text{N}(\text{metr})_2$  (4c)

| Radition | $\text{N}_2 + \text{Drug}$ | $\text{N}_2$ Time (64) | Radition | $\text{O}_2 + \text{Drug}$ | $\text{O}_2$ | Time   |
|----------|----------------------------|------------------------|----------|----------------------------|--------------|--------|
| 4' 18    | 20,000                     | 10,000                 | 4'       | 8                          | 10,000       | 10,000 |
| 6' 12    | 5000                       | 2000                   | 3' - 6   |                            | 5000         | 5000   |
| 3' 6     | 1000                       | 500                    | 2' 4     |                            | 1000         | 1000   |
| 0        | 200                        | 200                    | 0        |                            | 200          | 200    |

Plated cell in dish incubation 2.5 h then add Drug pump 1 h then put water bath  
 $37^\circ\text{C}$  1 hr <sup>then</sup> ~~✓~~ radiation Oxic in incubator

Drug:  $(\text{metr})_2\text{NCCl}_3(\text{metr})_2$  : 2.8.2.9/61.11.0001. Fw. 686.18 = 0.679 mM

7 days later, stained, counted

|      | $\text{O}_2 + \text{Drug}$ Count | mean  | SF         | SF/PE       |              |
|------|----------------------------------|-------|------------|-------------|--------------|
| 86f  | 0                                | 0     | 0          | 82.44.46    | 74           |
| 126f | 0                                | 0     | 0          | 125.129.130 | 124.7        |
| 66f  | 36.8.9                           | 17.7  | 0.0035     | 0.024       | 136.132.90   |
| 0    | 43.23.25                         | 30.3  | 0.15 (PE)  | 16.44.52    | 74           |
|      |                                  |       |            | 0.37 (PE)   |              |
|      |                                  | 82    |            |             |              |
|      |                                  |       |            |             | $\text{O}_2$ |
| 86f  | 704.219.204                      | 209   | 0.0209     | 0.038       | 227.224.232  |
| 66f  | 296.318.305                      | 306.3 | 0.061      | 0.11        | 328.314.311  |
| 116f | 192.168.187                      | 182.3 | 0.182      | 0.33        | 207.213.230  |
| 0    | 105.120.109                      | 111.3 | 0.557 (PE) | 118.130.155 | 134.3        |
|      |                                  |       |            | 0.67 (PE)   |              |

Taxol and Taxol-mitobenzine toxicity

| Taxol   | No. Count   | mean        | SF    | 1/2 = 22 Count | mean       | SF          | SF/PE |      |
|---------|-------------|-------------|-------|----------------|------------|-------------|-------|------|
| T-5     | 71.74.75    | 82.67       | 0.41  | 0.74           | 44.5.6     | 5           | 0.025 |      |
| T-6     | 82.75.71    | 76          | 0.38  | 0.63           | 25.25.19   | 23          | 0.115 |      |
| T-7     | 94.93.82    | 89.7        | 0.448 | 0.50           | 80.63.74   | 73.7        | 0.37  |      |
| T-8     | 128.110.118 | 118.7       | 0.59  | 1.06           | 49.115.132 | 129.3       | 0.65  |      |
| control | T-9         | 105.106.126 | 112.3 | 0.56           | 1.007      | 132.126.119 | 125.7 | 0.63 |

TNB = Taxol-mitobenzine

|       |               |       |            |               |          |            |       |
|-------|---------------|-------|------------|---------------|----------|------------|-------|
| TNB-5 | 0. 0. 0       | 0     | 0          | 0. 0. 0       | 0        | 0          | 0     |
| TNB-6 | 39. 49. 52    | 46.7  | 0.23       | 0.42          | 2. 2. 0  | 1.3        | 0.007 |
| TNB-7 | 91. 81. 96    | 89.3  | 0.447      | 0.80          | 40.19.32 | 30.3       | 0.15  |
| TNB-8 | 84. 98. 96    | 92.7  | 0.46       | 0.83          | 29.29.57 | 38.3       | 0.19  |
| TNB-9 | 102. 92. 102. | 98.7  | 0.49       | 0.88          | 66.70.50 | 62         | 0.31  |
| (2)   | 110. 111. 114 | 111.7 | 0.558 (PE) | 122. 119. 138 | 123      | 0.615 (PE) |       |

Each dish add 200 cell. plant 1 cell in dish incubator 6hr. then add drug pump/hr. after pump with chamber incubator 24hr. ofic in incubator.

Drug Taxol from 1mM  $\rightarrow$   $0.3\text{ml} + 29.7\text{ml} = 10^{-5}$

$$3\text{ml} + 27\text{ml} = 10^{-6}$$

$$3\text{ml} + 27\text{ml} = 10^{-7}$$

$$3\text{ml} + 27\text{ml} = 10^{-8}$$

$$3\text{ml} + 27\text{ml} = 10^{-9}$$

TNB 1mM  $\rightarrow$   $0.3\text{ml} + 29.7\text{ml} = 10^{-5}$

$$3\text{ml} + 27\text{ml} = 10^{-6}$$

$$3\text{ml} + 27\text{ml} = 10^{-7}$$

$$3\text{ml} + 27\text{ml} = 10^{-8}$$

$$3\text{ml} + 27\text{ml} = 10^{-9}$$

Radiosensitization of DPTM1 = 3C

| Time   | RT<br>( $\text{hr}$ ) | Hypoxic + Drug | $N_2$  | Time | RT<br>( $\text{hr}$ ) | $O_2 + \text{Drug}$ | $O_2$  |
|--------|-----------------------|----------------|--------|------|-----------------------|---------------------|--------|
| 4 4'5" | 18                    | 20,000         | 10,000 | 4'2" | 8                     | 10,000              | 10,000 |
| 6 6'0" | 12                    | 5000           | 2000   | 3'2" | 6                     | 5000                | 5000   |
| 3 3'2" | 6                     | 1000           | 5000   | 2'1" | 4                     | 1000                | 1000   |
|        | 0                     | 200            | 200    | 0    | 0                     | 200                 | 200    |

Plated cell in dish incubator 2.5/hr. then add Drug pump 1hr. after put Water bath

37°C 1hr <sup>then</sup> irradiation 0.1c in incubator. Drug  $\pm$  from DPTM1 = 3C

$$10.9 \text{ ml} + 7.2 \text{ ml} = 1 \text{ mM}$$

$$8 \text{ ml} + 7.2 \text{ ml} = 0.1 \text{ mM}$$

(Drug) (H255)

Count

|       | $N_2 + \text{Drug}$ Count | mean  | SF       | SF/PE  | $N_2$ Count | mean  | SF       | SF/PE |
|-------|---------------------------|-------|----------|--------|-------------|-------|----------|-------|
| 16.84 | 78.53.62                  | 64.3  | 0.003    | 0.0066 | 123.102.72. | 97    | 0.009    | 0.017 |
| 6.164 | 98.88.113                 | 49.7  | 0.02     | 0.0407 | 71.80.72.   | 74.3  | 0.037    | 0.073 |
| 6.64  | 118.126.135               | 126.3 | 0.126    | 0.258  | 132.85.79   | 98.7  | 0.20     | 0.39  |
| 0     | 102.92.98                 | 97.3  | 0.49(PE) |        | 114.84.110  | 102.7 | 0.51(PE) |       |

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|       | $O_2 + \text{Drug}$ | $O_2$        |
|-------|---------------------|--------------|
| 16.84 | 89.92.107           | 96           |
|       | 0.0096 0.092        | 162.152.149. |
| 0.664 | 143.170.170         | 161          |
|       | 0.0322 0.064        | 228.235.231  |
| 6.64  | 120.133.129         | 127.3        |
|       | 0.127 0.25          | 166.141.165  |
| 0     | 102.95.105          | 100.7        |
|       | 0.50(PE)            | 104.121.121  |
|       |                     | 115.3        |
|       |                     | 0.58(PE)     |

## DBTM + Radiation

## DBTM = 4C

from DBTM 4.647 mg/ml

| ne | RT<br>(gy) | N <sub>2</sub> +D | N <sub>2</sub> | RT<br>Time (gy) | C <sub>2</sub> +D | O <sub>2</sub> |
|----|------------|-------------------|----------------|-----------------|-------------------|----------------|
|    | 18         | 20,000            | 10,000         | 8               | 5000              | 5000           |
|    | 1264       | 5000              | 2000           | 6               | 2000              | 2000           |
|    | 6          | 1000              | 500            | 4               | 1000              | 1000           |
|    | 0          | 200               | 200            | 0               | 200               | 200            |

plate cell in dish 3.5 hr incubator. then add drug pump 1/hr. after pump put waterbath 37°C 1 hr. then radiation after wash off the drug. add new medium keep in incubator for 80's.

| N <sub>2</sub> +Drug Count | mean | SF     | SF/PE | N <sub>2</sub> Count | mean | SF     | SF/PE |
|----------------------------|------|--------|-------|----------------------|------|--------|-------|
| 46.35.35                   | 38.7 | 0.0019 | 0.006 | 101.91.30.           | 74   | 0.0074 | 0.053 |
| 47.81.127                  | 85   | 0.017  | 0.053 | 83.49.51             | 61   | 0.0305 | 0.22  |
| 77.83.124                  | 94.7 | 0.095  | 0.3   | 29.22.82             | 44.3 | 0.09   | 0.63  |
| 73.32.88                   | 64.3 | 0.32   | (PE)  | 42.25.15             | 27.3 | 0.14   | (PE)  |

O<sub>2</sub>+DrugO<sub>2</sub>

|             |       |       |       |             |       |       |      |
|-------------|-------|-------|-------|-------------|-------|-------|------|
| 84.53.73    | 70    | 0.014 | 0.026 | 104.97.87   | 96    | 0.019 | 0.03 |
| 110.129.116 | 118.3 | 0.059 | 0.106 | 150.141.151 | 147.3 | 0.074 | 0.12 |
| 164.154.161 | 159.7 | 0.16  | 0.29  | 159.173.176 | 169.3 | 0.17  | 0.28 |
| 120.110.106 | 112   | 0.56  | (PE)  | 120.136.110 | 122   | 0.61  | (PE) |

X

## CTM = 5C      Toxicity Experiment

|      |         | At   |
|------|---------|------|
| C 1. | 101.48  | 0.23 |
| C 2. | 110.106 | 19.5 |
| C 3. | 108.124 | 6.12 |

120.136.180      0.61 (PE)      42.25.15      0.14 (PE)

Plated CEM in dish. 3.5 hr incubator. Each dish add 200 cells.

↓  
add drug pump 1 hr. then waterbath 1 hr.

$$SC = 0.15 \text{ ml} + 14.85 \text{ ml (HBSS)} = 1 \text{ mM. SC1.}$$

$$↓  
1.5 \text{ ml} + 13.5 \text{ ml HBSS} = 0.1 \text{ mM. SC2.}$$

$$↓  
1.5 \text{ ml} + 13.5 \text{ ml HBSS} = 0.01 \text{ mM. SC3.}$$

CTM = 5C + Radiation

|                        | $N_2$  | $N_2$             | $O_2 + Drug$ | $O_2$ |
|------------------------|--------|-------------------|--------------|-------|
| (Gy) 86 <sup>1/2</sup> | 20.000 | 86 <sup>1/2</sup> | 10.000       | 5000  |
| 126 <sup>1/2</sup>     | 5000   | 2000              | 6 2000       | 1000  |
| 66 <sup>1/2</sup>      | 1000   | 500               | 4 1000       | 500   |
| 0                      | 200    | 200               | 0 200        | 200   |

Drug: from CPM = 5C  $0.15 \text{ ml} + 14.88 \text{ ml} = 1 \text{ mM}$

$0.075 \text{ ml} + 75 \text{ ml} = 0.1 \text{ mM}$   
(x2) HBSS

plated cell in dish 2.5 hr. incubator. Then add drug pump hr. Then water bath 1hr 37°C, then radiation.

| $N_2 + Drug$ Count | mean  | SF       | SF/PE | $N_2$ Count | mean  | SF       | SF/PE |
|--------------------|-------|----------|-------|-------------|-------|----------|-------|
| 38.44.19           | 33.7  | 0.0017   | 0.003 | 158.195.164 | 172.3 | 0.017    | 0.025 |
| 62.72.44           | 76    | 0.0152   | 0.028 | 157.127.119 | 134.3 | 0.067    | 0.099 |
| 159.143.??         | 124.7 | 0.12     | 0.23  | 154.155.173 | 160.7 | 0.32     | 0.47  |
| 109.108.109        | 108.7 | 0.54(PE) |       | 136.132.140 | 136   | 0.68(PE) |       |

$O_2 + Drug$

|                               |       |          |       | $O_2$       |       |          |       |
|-------------------------------|-------|----------|-------|-------------|-------|----------|-------|
| 86 <sup>1/2</sup> 148.232.215 | 215   | 0.0215   | 0.032 | 99.113.95   | 102.3 | 0.02     | 0.031 |
| 66 <sup>1/2</sup> 140.156.1-9 | 141.7 | 0.071    | 0.106 | 67.64.80    | 70.3  | 0.07     | 0.107 |
| 66 <sup>1/2</sup> 158.181.150 | 163   | 0.163    | 0.24  | 113.104.99  | 105.3 | 0.21     | 0.319 |
| 0 128.139.124                 | 133.7 | 0.67(PE) |       | 144.124.128 | 132   | 0.66(PE) |       |

## Taxol and Taxol-nitrobenzine toxicity

|       | No   | Count | mean | SF         | SF/PE | O <sub>2</sub> | Count   | mean | SF        | SF/PE |
|-------|------|-------|------|------------|-------|----------------|---------|------|-----------|-------|
| T-5   | dish | 43.52 | 47.5 | 0.2375     | 0.62  | 2dish          | 5.10    | 7.5  | 0.0375    | 0.07  |
| T-6   | "    | 46.53 | 49.5 | 0.2475     | 0.647 | "              | 13.2    | 19.5 | 0.0975    | 0.17  |
| T-7   | "    | 95.93 | 94   | 0.47       | 1.23  | "              | 72.5    | 61   | 0.35      | 0.53  |
| T-8   | "    | 74.73 | 73.5 | 0.3675     | 0.96  | "              | 127.121 | 124  | 0.62      | 1.08  |
| T-9   | "    | 30.80 | 80   | 0.4        | 1.05  | "              | 46.114  | 105  | 0.535     | 0.91  |
| O     | "    | 74.79 | 76.5 | 0.3825(PE) | "     | "              | 135.105 | 115  | 0.575(PE) | "     |
| TNB-5 | "    | 0     | 0    | 0          | "     | "              | 0       | 0    | 0         | 0     |
| TNB-6 | "    | 33.20 | 26.5 | 0.1325     | 0.35  | "              | 1.3     | 2    | 0.01      | 0.017 |
| TNB-7 | "    | 63.77 | 73   | 0.3805     | 0.74  | "              | 57.25   | 26.0 | 0.185     | 0.48  |
| TNB-8 | "    | 69.77 | 73   | 0.365      | 0.95  | "              | 55.58   | 56.5 | 0.28      | 0.49  |
| TNB-9 | "    | 81.81 | 81   | 0.405      | 1.06  | "              | 90.84   | 87   | 0.435     | 0.76  |

Each dish add 200 cell. put incubator 6hr. then add drug. Hypoxic pump 1hr. then with chamber put incubator 24hr. or in incubator 24hr. after wash off the drug.

$$\text{Taxol: } 0.2 + 19.8 = 10^{-5}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-6}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-7}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-8}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-9}$$

$$\text{TNB: } 0.2 + 19.8 ml = 10^{-5}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-6}$$

$$\downarrow$$

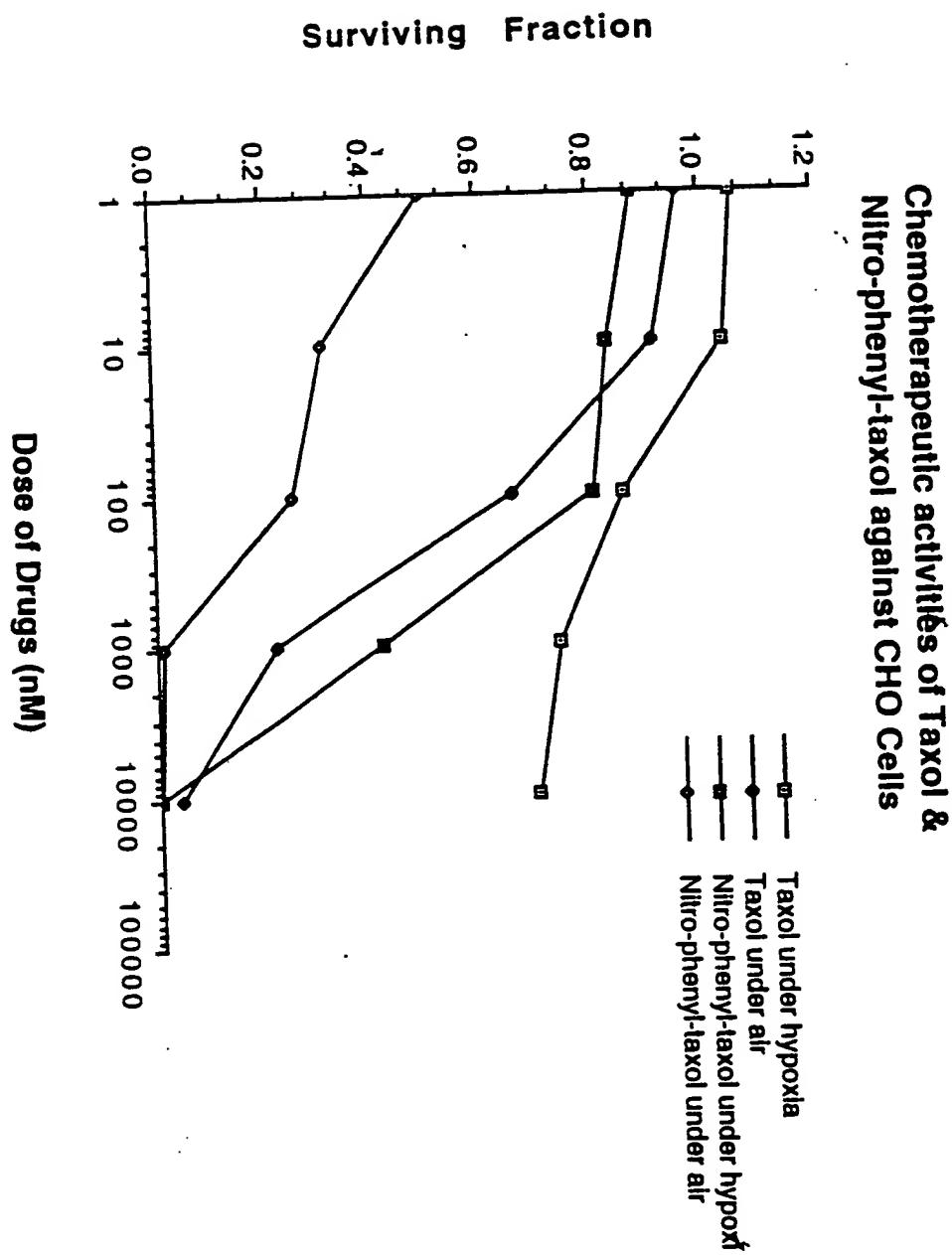
$$2ml + 18ml = 10^{-7}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-8}$$

$$\downarrow$$

$$2ml + 18ml = 10^{-9}$$



DBTM =  $4C + \text{Radiation}$ DBTM =  $0.1 \text{ mM}$ 

| Time (GY) | $N_2$  | $O_2 + \text{Drug}$ | $O_2$  |
|-----------|--------|---------------------|--------|
| 18        | 20,000 | 10,000              | 8,5000 |
| 12        | 5000   | 7000                | 6,2000 |
| 6         | 1000   | 500                 | 4,1000 |
| 0         | 200    | 200                 | 0,200  |

Drug: from  $9.697 \text{ mM}$ .

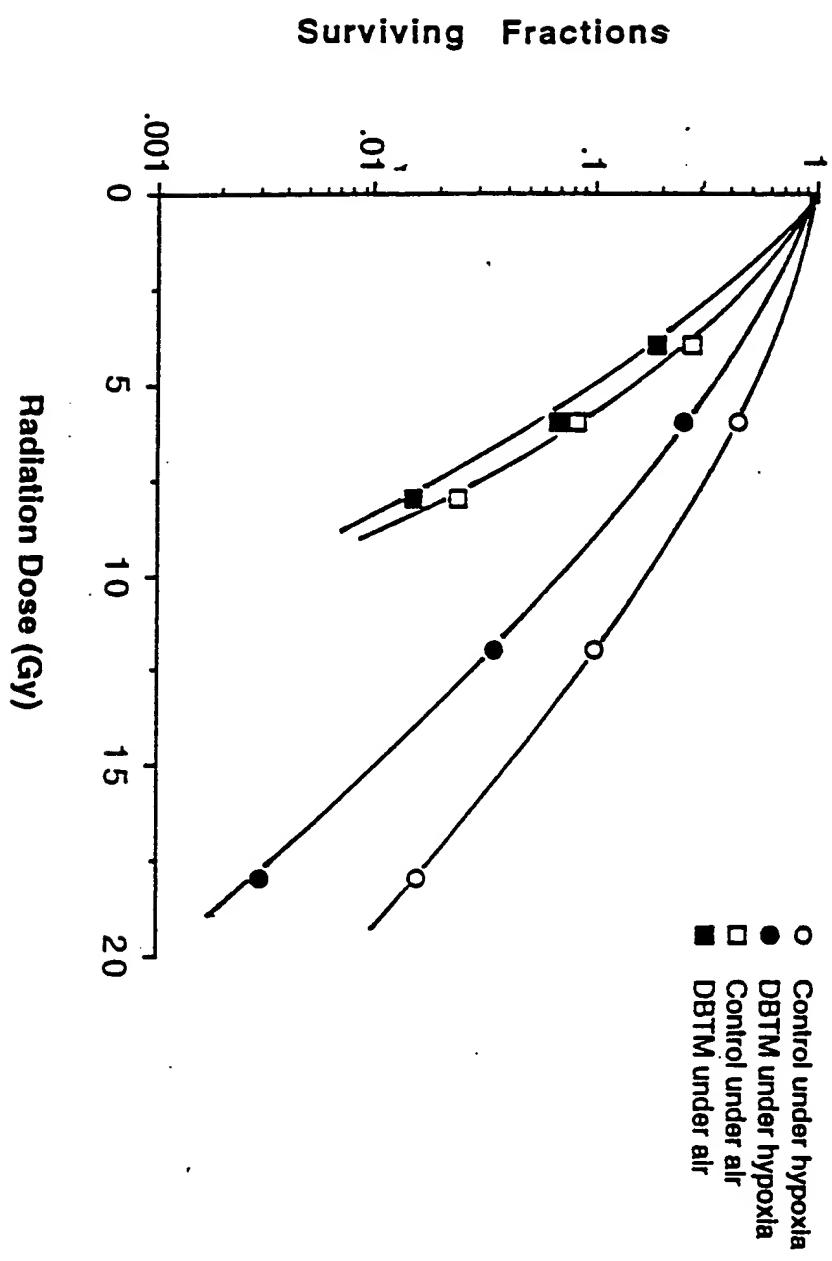
$$1.62 - e + 73.4 = 0.2 \text{ mM}$$

Plated cell in dish 2.5 hr incubator then add drug pump 1hr. then put waterbath  $37^\circ\text{C}$   
 1hr.oxic in incubator. after radiation

| $N_2 + D$ count | mean        | SF    | $S/\text{PE}$ | $N_2$ count | mean        | SF    | $S/\text{PE}$ |       |
|-----------------|-------------|-------|---------------|-------------|-------------|-------|---------------|-------|
| 8Gf             | 30.38.29    | 32.3  | 0.0016        | 0.00291     | 83.86.94    | 87.7  | 0.0088        | 0.016 |
| 16f             | 106.43.88   | 45.7  | 0.019         | 0.035       | 122.109.106 | 112.3 | 0.056         | 0.1   |
| 6Gf             | 119.149.144 | 137.3 | 0.137         | 0.25        | 131.126.113 | 123.3 | 0.25          | 0.44  |
| 0               | 45.110.98   | 107.7 | 0.54 (PE)     |             | 120.103.115 | 112.3 | 0.56 (PE)     |       |

| $O_2 + D$ count |             | $O_2$ count |           |
|-----------------|-------------|-------------|-----------|
| 8Gf             | 03.39.43    | 41.7        | 0.008     |
|                 |             | 61. 61.58   | 60        |
|                 |             | 0.012       | 0.024     |
| 6Gf             | 68.79.72    | 73          | 0.0365    |
|                 |             | 40. 39.49   | 42.7      |
|                 |             | 0.043       | 0.084     |
| 4Gf             | 105.101.97  | 101         | 0.101     |
|                 |             | 58. 74.75   | 69        |
|                 |             | 0.138       | 0.27      |
| 0               | 103.113.110 | 108.7       | 0.54 (PE) |
|                 |             | 115. 95.94  | 101.3     |
|                 |             | 0.51 (PE)   |           |

### Radiosensitizing effects of DBTM (0.1 mM) on CHO Cells



CTM = 5C + Radiation

CTM = 0.1 mM

| Radiation                      | N <sub>2</sub> + Drug | RT | N <sub>2</sub> (C <sub>6</sub> ) | C <sub>2</sub> + Drug | O <sub>2</sub> |
|--------------------------------|-----------------------|----|----------------------------------|-----------------------|----------------|
| (C <sub>6</sub> ) <sub>2</sub> | N <sub>2</sub> + Drug |    | N <sub>2</sub> (C <sub>6</sub> ) | C <sub>2</sub> + Drug | O <sub>2</sub> |
| 18                             | 20,000                |    | 10,000                           | 8                     | 10,000         |
| 12                             | 5000                  |    | 2000                             | 6                     | 2000           |
| 6                              | 1000                  |    | 500                              | 4                     | 1000           |
| 0                              | 200                   |    | 200                              | 0                     | 200            |

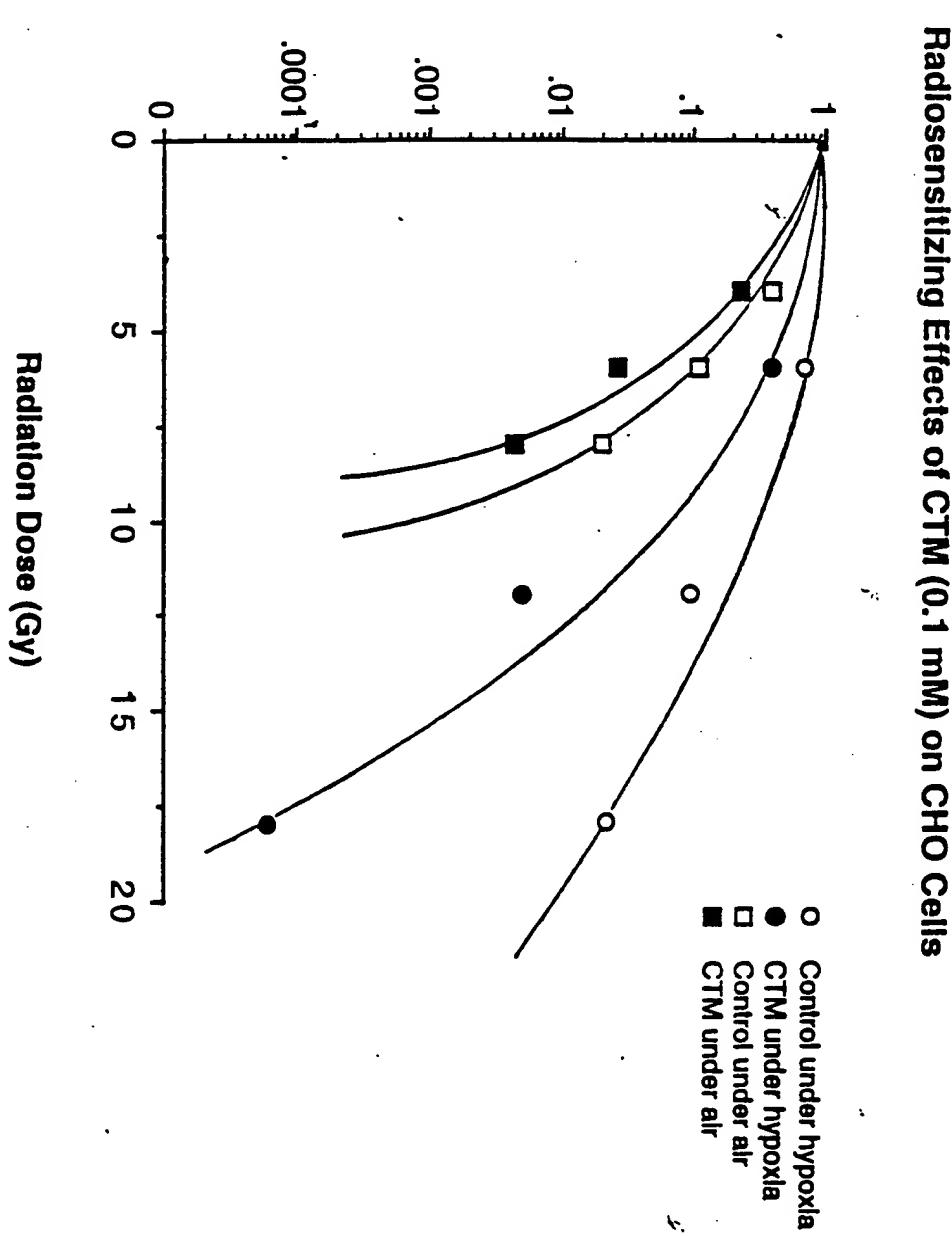
Drug: from 100 mM

$$0.076 \text{ mL} + 75 \text{ mL} = 0.1 \text{ mM}$$

Plated cell in dish incubator 3.5 hr then add drug pump/hr. after post water bath  
<sup>(HBSS)</sup>  
 37°C 1 hr. radiationoxic working in incubator.

| N <sub>2</sub> + Drug Count | mean        | SF    | SF/PE    | N <sub>2</sub> Count | mean        | SF    | SF/PE    |       |
|-----------------------------|-------------|-------|----------|----------------------|-------------|-------|----------|-------|
| 18C <sub>6</sub>            | 1.0.0.      | 0.3   | 0.00002  | 0.00006              | 114.109.95  | 106   | 0.0106   | 0.022 |
| 12C <sub>6</sub>            | 6.7.8       | 7     | 0.0014   | 0.005                | 83.113.83   | 93    | 0.0465   | 0.097 |
| 6C <sub>6</sub>             | 101.104.123 | 109.3 | 0.109    | 0.4                  | 166.162.166 | 164.7 | 0.33     | 0.69  |
| 0                           | 68.45.48    | 53.7  | 0.27(PE) |                      | 100.88.99   | 95.7  | 0.48(PE) |       |

| O <sub>2</sub> Count |            |      |          |
|----------------------|------------|------|----------|
| 8C <sub>6</sub>      | 22.18.16   | 18.7 | 0.0019   |
| 6C <sub>6</sub>      | 27.16.25   | 22.7 | 0.011    |
| 4C <sub>6</sub>      | 78.107.115 | 100  | 0.1      |
| 0                    | 88.108.63  | 86.3 | 0.43(PE) |



## CTM=5C + Radiation

| Rad  | CTM  | RT     | O <sub>2</sub> + Drug | O <sub>2</sub> |
|------|------|--------|-----------------------|----------------|
| (Ct) | (Ct) | (Ct)   | (Ct)                  | (Ct)           |
| 1    | 18   | 20.000 | 10.000                | 8              |
| 12   | 5000 | 2000   | 6                     | 1000           |
| 6    | 1000 | 500    | 4                     | 500            |
| 0    | 200  | 200    | 0                     | 200            |

CTM = 0.1 mM

Drug: from 100 mM

$$0.076 \text{ ml} + 75 \text{ ml} = 0.1 \text{ mM}$$

Plated cell in dish incubator 3 hr, add drug pump 1 hr, then put water bath 37°C 1 hr.  
then radiationoxic in incubator.

|     | N <sub>2</sub> +Drug Count | mean         | SF      | SF/PE     | N <sub>2</sub> Count | mean          | SF    | SF/PE      |       |
|-----|----------------------------|--------------|---------|-----------|----------------------|---------------|-------|------------|-------|
| 186 | 1. 7. 2.                   | 3.3          | 0.00017 | 0.0003    | 140. 145. 166        | 150           | 0.05  | 0.025      |       |
| 126 | 18. 6. 1                   | 25. 15. 40   | 26.7    | 0.0053    | 0.01                 | 151. 145. 121 | 139   | 0.0695     | 0.114 |
| 66  | 6. 6. 1                    | 134. 97. 106 | 112.3   | 0.112     | 0.26                 | 144. 158. 158 | 153.3 | 0.31       | 0.5   |
| 0   | 0                          | 99. 110. 104 | 104.3   | 0.52 (PE) |                      | 123. 110. 132 | 121.7 | 0.608 (PE) |       |

O<sub>2</sub> Count

|    |    |               |       |       |       |               |      |           |       |
|----|----|---------------|-------|-------|-------|---------------|------|-----------|-------|
| 86 | 86 | 98. 118. 104  | 106.7 | 0.02  | 0.03  | 121. 117. 107 | 115  | 0.023     | 0.03  |
| 66 | 66 | 81. 58. 80    | 73    | 0.073 | 0.114 | 61. 76. 57    | 64.7 | 0.065     | 0.095 |
| 46 | 46 | 126. 104. 107 | 112.3 | 0.225 | 0.35  | 122. 121. 111 | 118  | 0.736     | 0.35  |
| 0  | 0  | 124. 140. 121 | 128.3 | 0.64  | (PE)  | 138. 135. 135 | 136  | 0.68 (PE) |       |

Taxol and Taxol nitrobenzine toxicity

|       | N       | mean | SE | S/PE | O <sub>2</sub> | mean | SE | S/PE |
|-------|---------|------|----|------|----------------|------|----|------|
| T-5   | 12.16   |      |    |      | 7.5            |      |    |      |
| T-6   | 29.21   |      |    |      | 9.11           |      |    |      |
| T-7   | 74.105  |      |    |      | 80.70          |      |    |      |
| T-8   | 79.74   |      |    |      | 147.104        |      |    |      |
| T-9   | 111.89  |      |    |      | 117.127        |      |    |      |
| O     | 120.106 |      |    |      | 130.109        |      |    |      |
| TNB-5 | 0       | 0    |    |      | 0              | 0    |    |      |
| TNB-6 | 33.33   |      |    |      | 1.4            |      |    |      |
| TNB-7 | 81.73   |      |    |      | 24.36          |      |    |      |
| TNB-8 | 84.94   |      |    |      | 56.82          |      |    |      |
| TNB-9 | 90.120  |      |    |      | 85.53          |      |    |      |

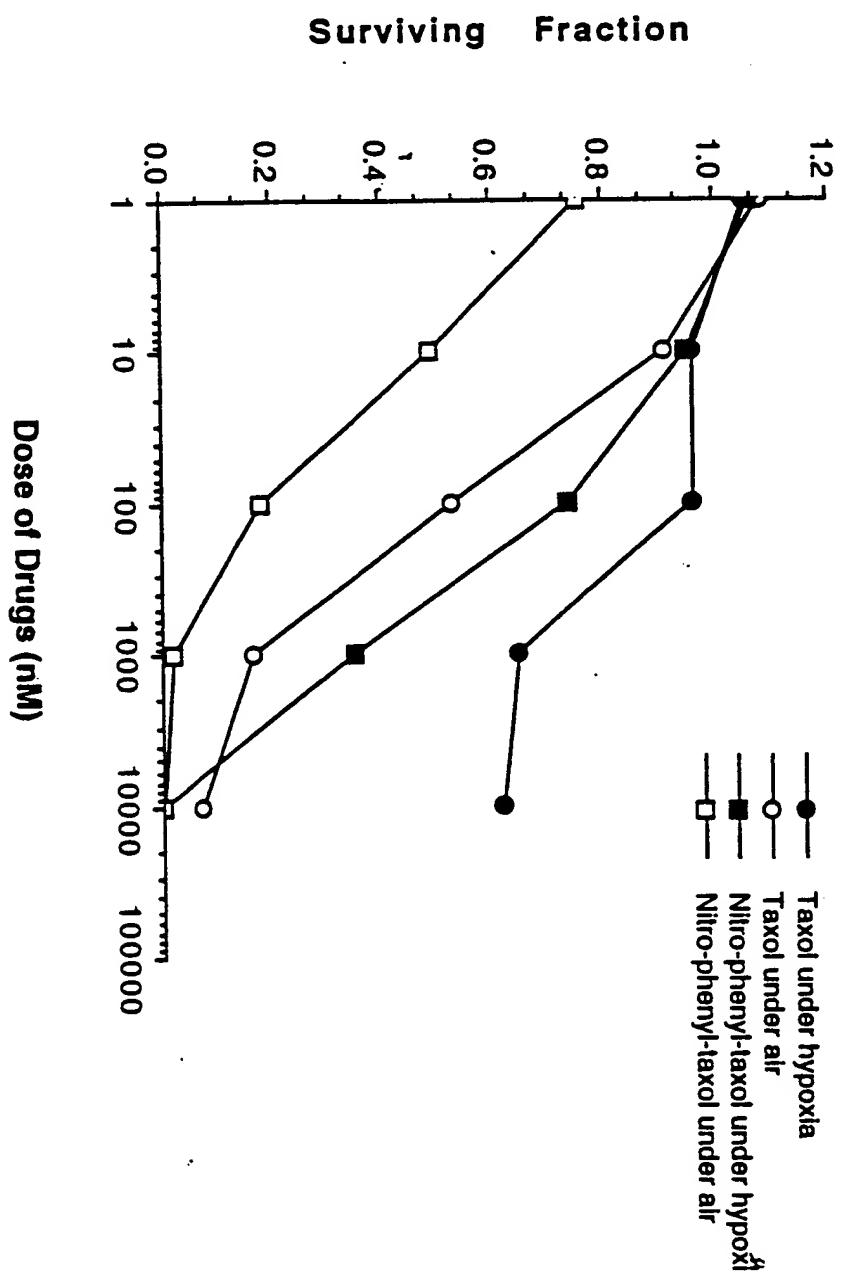
T = Taxol      TNB = Taxol nitrobenzine

Each dish plated 200 cells in incubator 6hr. then add drug hypoxic pump 1hr. then with chamber put incubator 24hr. toxic add drug incubator 24hr.

$$\begin{aligned}
 \text{Drug from: Taxol: } & 0.2 \text{ ml} + 18 \text{ ml} = 10^{-5} \\
 & \downarrow \text{(medium)} \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-6} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-7} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-8} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-9}
 \end{aligned}$$

$$\begin{aligned}
 \text{TNB: } & 22 \text{ ml} + 19.8 \text{ ml} = 10^{-5} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-6} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-7} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-8} \\
 & \downarrow \\
 & 2 \text{ ml} + 18 \text{ ml} = 10^{-9}
 \end{aligned}$$

Chemotherapeutic Activities of Taxol &  
Nitro-phenyl-taxol against CHO Cells



## [2101-mitor + Radiation]

| (RT)<br>(Time) | RT<br>12+10ug | 12<br>1hr | RT<br>(4) | C2+D10ug<br>1hr | O2   |
|----------------|---------------|-----------|-----------|-----------------|------|
| 18             | 22.600        | 10.000    | 3         | 5000            | 2000 |
| 12             | 5000          | 2000      | 6         | 2000            | 1000 |
| 6              | 1000          | 500       | 4         | 1000            | 500  |
| 0              | 200           | 200       | 0         | 700             | 200  |

placed cell in dish incubator 6hr then add drug pump 1hr stic in incubator  
after pump with chamber put incubator 24hr then radiation.

Drug: Taxol-mg/100ml

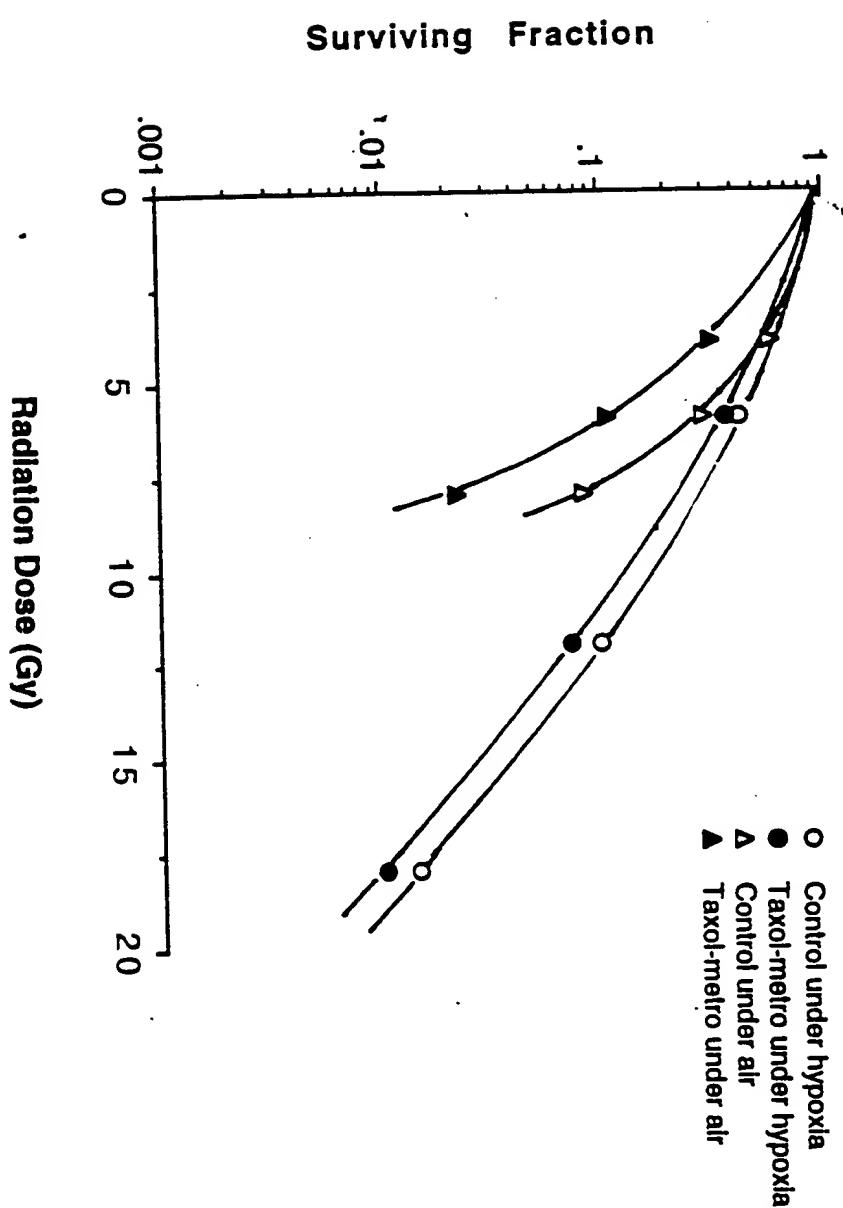
$$20\text{ ml} + 1.48\text{ ml} = 10^{-5}$$

↓ (medium)

$$10\text{ ml} + 1.44\text{ ml} = 10^{-7}$$

|       | N1 + D Count    | mean  | SF        | SF/PE | N2 Count    | mean  | SF         | SF/PE |
|-------|-----------------|-------|-----------|-------|-------------|-------|------------|-------|
| -180f | 110.139.115     | 121.3 | 0.006     | 0.01  | 118.96.84   | 99.3  | 0.0099     | 0.014 |
| -120f | 216.227.209     | 217.3 | 0.043     | 0.070 | 129.144.157 | 143.3 | 0.072      | 0.1   |
| -60f  | 178.239.229     | 215.3 | 0.215     | 0.365 | 152.167.178 | 152.3 | 0.3        | 0.429 |
| -0    | 126.103.126     | 118.3 | 0.59 (PE) |       | 139.147.138 | 141.3 | 0.71 (PE)  |       |
|       | C2 + Drug Count | mean  | SF        | SF/PE | C2 Count    | mean  | SF         | SF/PE |
| -80f  | 12.16.12.       | 13.3  | 0.003     | 0.022 | 127.129.108 | 121.3 | 0.06       | 0.085 |
| -60f  | 25.27.30        | 27.3  | 0.04      | 0.11  | 214.207.226 | 215.7 | 0.216      | 0.3   |
| -40f  | 31.35.50        | 38.7  | 0.039     | 0.52  | 259.216.217 | 214   | 0.428      | 0.599 |
| -0    | 24.27.23        | 24.7  | 0.12 (PE) |       | 143.135.148 | 143   | 0.715 (PE) |       |

### Radiosensitization of Taxol-metro (100nM) on CHO Cells (1st exp)



| 7.3.80 - Nitrobenzine + Radiation |                     | TVB $10^{-3}$ ml |                     |       |
|-----------------------------------|---------------------|------------------|---------------------|-------|
| (RT)                              | $N_2 + \text{Drug}$ | (RT)             | $C_2 + \text{Drug}$ | $C_2$ |
| 18                                | 2000                | 10000            | 8                   | 5000  |
| 12                                | 5000                | 2000             | 6                   | 2000  |
| 6                                 | 1000                | 500              | 4                   | 1000  |
| 0                                 | 200                 | 200              | 0                   | 200   |

placed cell in dish 5.5 hr then add drug, pump 1 hr after pump with chamber put in incubator 24 hr at 37°C incubator. then radiation.

$$\text{Dose: from TVB } 10^{-3} \rightarrow 0.32 \text{ ml} + 1.48 \text{ ml} = 10^{-5} \rightarrow 1 \text{ ml} + 9 \text{ ml} = 10^{-6} \rightarrow 10 \text{ ml} + 90 \text{ ml} = 10^{-7}$$

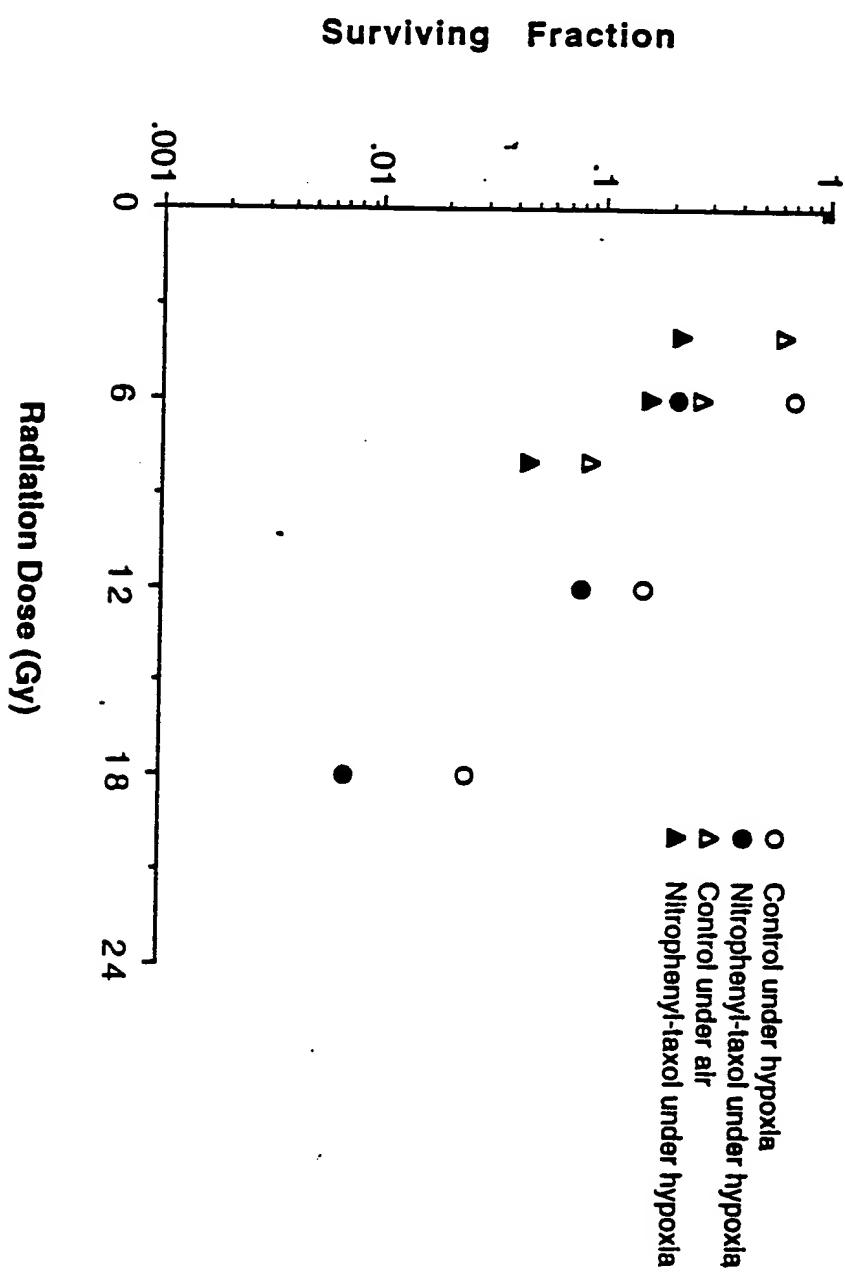
(medium)

| $N_2 + \text{Drug}$ Count | mean  | SF        | $S/\sigma$ | $N_2$ Count | mean  | SF        | $S/\sigma$ |
|---------------------------|-------|-----------|------------|-------------|-------|-----------|------------|
| 607 60.79.65              | 68    | 0.0034    | 0.007      | 152.183.169 | 168   | 0.0168    | 0.025      |
| 1267 241.170.220          | 210.3 | 0.042     | 0.082      | 244.189.221 | 204.7 | 0.102     | 0.153      |
| 667 115.113.99            | 104   | 0.107     | 0.21       | 254.226.226 | 235.3 | 0.47      | 0.7        |
| 0 99.98.108               | 101.7 | 0.51 (PE) |            | 130.129.145 | 134.7 | 0.67 (PE) |            |

| $C_2 + \text{Drug}$ Count | $C_2$ Count |
|---------------------------|-------------|
| 50.45.60                  | 51.7        |
| 667 72.71.70              | 71          |
| 467 42.56.53              | 50.3        |
| 0 49.44.42                | 45          |

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Radiosensitizing Effects of Nitro-phenyl-taxol (100 nM) on CHO Cells



## Taxol + Radiation

## 2T Hypoxic + Drug

18 2000

12 5000

6 1000

0 200

## Hypoxic RT Otic + b. 2%

10.000 8 5000

2000 6 - 2000

500 4 1000

200 0 200

 $I = 10^{-5}$ 

## Otic

2000

1000

500

200

Plated cell in dish 1 hr incubator. then add drug pump 1 hr. after pump with chamber incubator 24 hr. then radiation otic in incubator.

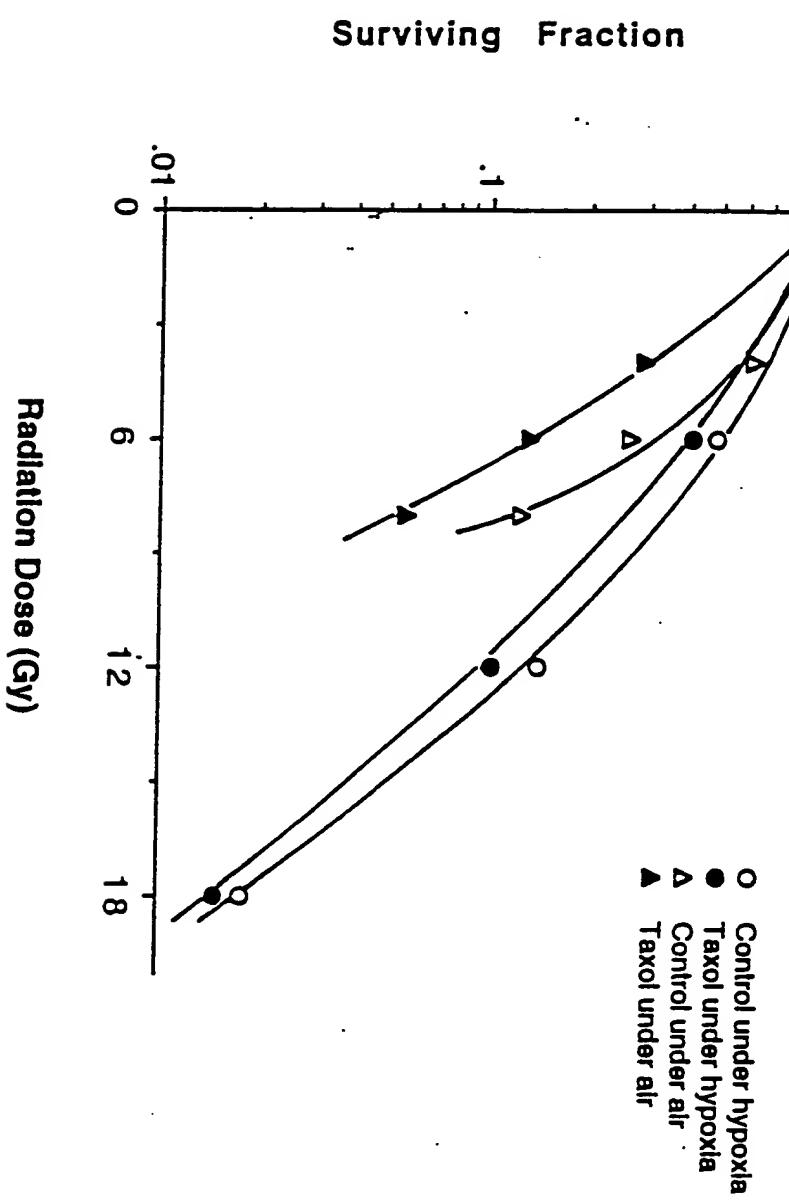
Drug: from Taxol  $10^{-3}$   $0.5 \text{ ml} + 4.5 \text{ ml} = 10^{-5}$   
 $\downarrow (\text{medium})$   
 $500 \text{ ml} + 500 \text{ ml} = 10^{-6}$

| $\text{N}^2 + \text{Drug}$ Count | Mean  | SF    | SF/PE | $\text{N}^2$ Count | Mean  | SF    | SF/PE |
|----------------------------------|-------|-------|-------|--------------------|-------|-------|-------|
| 9.64 (10. 11. 12)                | 125   | 0.006 | 0.015 | 105. 130. 90       | 108.3 | 0.011 | 0.018 |
| 12.64 (23. 24. 19)               | 220.3 | 0.044 | 0.102 | 174. 161. 172      | 169   | 0.085 | 0.143 |
| 6.64 (49. 17. 19)                | 173.7 | 0.174 | 0.404 | 148. 141. 137      | 142   | 0.284 | 0.481 |
| 0 85. 102. 70                    | 85.7  | 0.43  | (PE)  |                    |       |       |       |

 $\text{O}_2 + \text{Drug}$  Count

|                   |      |       |       |               |       |       |       |
|-------------------|------|-------|-------|---------------|-------|-------|-------|
| 8.64 (5. 26. 32)  | 34.3 | 0.007 | 0.057 | 116. 161. 148 | 151.7 | 0.076 | 0.124 |
| 6.64 (39. 35. 22) | 32   | 0.016 | 0.133 | 172. 159. 154 | 161.7 | 0.162 | 0.265 |
| 4.64 (38. 39. 27) | 34.7 | 0.035 | 0.289 | 191. 186. 194 | 190.3 | 0.381 | 0.624 |
| 0 26. 18. 29      | 24.3 | 0.12  | (PE)  | 119. 116. 133 | 122.7 | 0.61  | (PE)  |

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Radiosensitizing Effects of Taxol (5  $\mu$ M) on CHO Cells



## SC PLDR Experiment

$$\frac{D_{1-0}}{D_{0-0}} = 0.1 \text{ m}^{-1} \text{f}$$

$$RT = 30^\circ\text{f}$$

|            |      |                |      |
|------------|------|----------------|------|
| 0 hours RT | 5000 |                |      |
| 2 hr RT    | 2000 | 2 hr RT + drug | 200  |
| 4 hr RT    | 1000 | 4 hr RT + drug | 1000 |
| 6 hr RT    | 500  | 6 hr RT + drug | 500  |
|            |      | 6 hr drug      | 200  |

Plated cells each dish  $2 \times 10^5$  3 days later (total 16 dishes) take 3 dishes add drug. 7 dishes  
 8 Gy of x-ray radiation 4: after RT. 3 dish add drug. 3 dish no drug. put incubator. 2 hr. 4 hr. 6 hr.  
 trypsin then plated cell in dish. incubator 8 day.

Drug: from 100 mM

$$0.02 \text{ ml} + 3.8 \text{ ml} = 4 \text{ ml. each dish add } 0.5 \text{ ml}$$

(HES)

$$0 + 2 \text{ ml } \text{dd Medium. total } 2.5 \text{ ml}$$

| Count               | mean  | SE    | SE/PE |
|---------------------|-------|-------|-------|
| 2 hr D 122.118.125. | 121.7 | 0.61  | 0.83  |
| 4 hr D 134.113.134. | 127   | 0.635 | 0.87  |
| 6 hr D 129.134.129. | 130.7 | 0.65  | 0.89  |
| 0 154.136.147.      | 145.7 | 0.73  | (PE)  |

## SC and Metor Toxicity

|    | $N_2$    | $O_2$    | $N_2$       | $O_2$    |                          |
|----|----------|----------|-------------|----------|--------------------------|
| C1 | 3 dishes | 3 dishes | M1 3 dishes | 3 dishes | $SC_1 = 1 \text{ mM}$    |
| C2 | 3 dishes | "        | M2 "        | "        | $SC_2 = 0.1 \text{ mM}$  |
| C3 | 3 dishes | "        | M3 "        | "        | $SC_3 = 0.01 \text{ mM}$ |

Plated cell in dish incubator 3.5 hr. then add drug ofic and Hypoxic.  $M_3 = \text{Metor } 1 \text{ mM}$   
 Hypoxic pump 1 hr. after pump put Waterbath  $37^\circ\text{C}$  1 hr. then wash out drug. add new  
 medium. incubation 7 days. Drug from  $SC$  to  $mm$   $\rightarrow 0.2 \text{ ml} + 19.8 = 1 \text{ mM}$   
 $\downarrow$  (HBS)

$$\text{Metor: } 136 \text{ mg} / 40 \text{ ml HBS} = 70 \text{ mM}$$

$$\downarrow$$

$$1 \text{ ml} + 1 \text{ ml} = 10 \text{ mM}$$

$$\downarrow$$

$$2 \text{ ml} + 18 \text{ ml} = 1 \text{ mM}$$

|                | $N_2$ Count | mean  | SE    | SE/PE | $O_2$ Count | mean  | SE    | SE/PE |
|----------------|-------------|-------|-------|-------|-------------|-------|-------|-------|
| 1 mM $SC_1$    | 0 0 0       |       |       |       | 0 0 0       |       |       |       |
| 0.1 mM $SC_2$  | 124.141.124 | 129.7 | 0.65  | 1.137 | 133.116.138 | 129   | 0.645 | 1.008 |
| 0.01 mM $SC_3$ | 128.127.129 | 128   | 0.64  | 1.123 | 129.146.137 | 137   | 0.685 | 1.07  |
| O Control      | 115.112.114 | 113.7 | 0.57  | (PE)  |             |       |       |       |
| 20 mM M1       | 117.99.111  | 109   | 0.545 | 0.46  | 130.146.103 | 126.3 | 0.63  | 0.99  |
| 10 mM M2       | 128.107.118 | 117.7 | 0.59  | 1.03  | 136.133.125 | 131.3 | 0.66  | 1.026 |
| 1 mM M3        | 96.135.123  | 118   | 0.59  | 1.035 | 133.145.128 | 135.3 | 0.68  | 1.057 |

| Taxol-motor + Radiation |                | CHO Cell   |                       | $D_{Drug} = 10^{-7}$ |
|-------------------------|----------------|------------|-----------------------|----------------------|
| N <sub>2</sub> + Drug   | A <sub>2</sub> | RT<br>(64) | O <sub>2</sub> + Drug | O <sub>2</sub>       |
| 20.000                  | 10.000         | 8          | 5000                  | 2000                 |
| 2000                    | 2000           | 6-         | 2000                  | 500                  |
| 500                     | 500            | 4          | 1000                  | 200                  |
| 200                     | 200            | 0          | 200                   | 200                  |

plate cell in dish 3 hr. incubator. then add drug.oxic in incubator. hypoxic pump 1/hr.  
after pump. put waterbath 37°C 1/hr. then radiation. after wash out the drug. put new  
medium. incubator 7 day. later. stain

Drug from:  $10^{-3}$

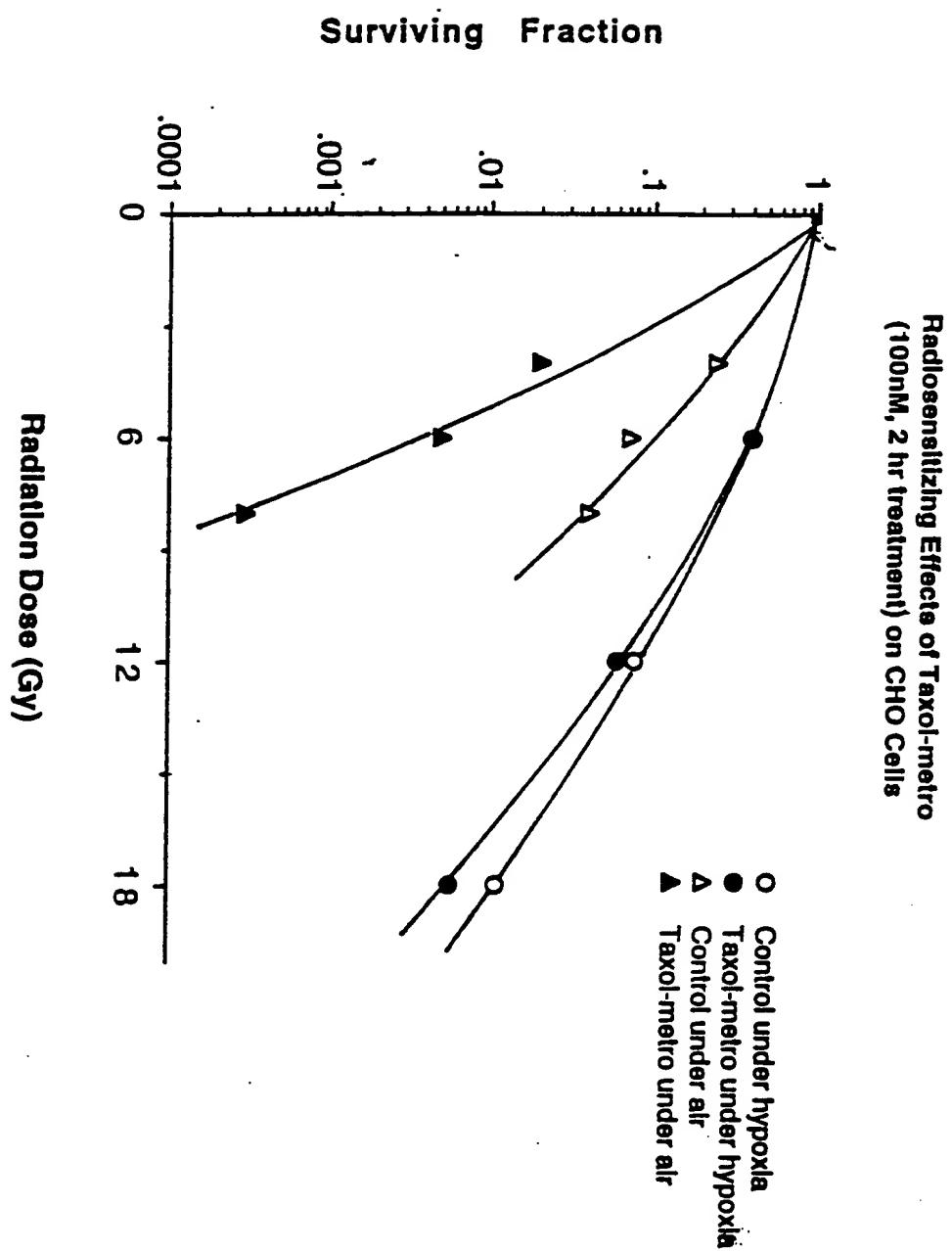
$$20\text{nl} + 1.98\text{ nl} = 10^{-5} \rightarrow 0.8\text{nl} + 7.2\text{nl} = 10^{-6} \rightarrow 8\text{nl} + 72\text{nl} = 10^{-7}$$

CH<sub>3</sub>SS

| N-Count         | mean  | SF        | SE/PE | N <sub>2</sub> + Drug Count | mean  | SF        | SE/PE  |
|-----------------|-------|-----------|-------|-----------------------------|-------|-----------|--------|
| 867 49.61.85    | 65    | 0.005     | 0.011 | 189 101.79.22               | 67.3  | 0.003     | 0.0057 |
| 267 113.94.83   | 96.7  | 0.048     | 0.078 | 100.79.73                   | 84    | 0.042     | 0.071  |
| 667 119.130.119 | 122.7 | 0.25      | 0.40  | 136.108.141                 | 128.3 | 0.26      | 0.435  |
| 0 132.127.112   | 123.7 | 0.62 (PE) |       | 125.128.103                 | 118.7 | 0.59 (PE) |        |

O<sub>2</sub> Count

| O <sub>2</sub> Count | mean | SF        | SE/PE | O <sub>2</sub> + Drug | mean | SF        | SE/PE  |
|----------------------|------|-----------|-------|-----------------------|------|-----------|--------|
| 867 51.56.63         | 56.7 | 0.028     | 0.041 | 0.1.0                 | 0.3  | 0.00026   | 0.0003 |
| 667 30.17.30         | 25.7 | 0.05      | 0.072 | 3.0.4.                | 2.3  | 0.001     | 0.005  |
| 667 38.25.44         | 35.7 | 0.18      | 0.25  | 8.3.3                 | 4.7  | 0.0047    | 0.02   |
| 0 153.132.141        | 142  | 0.71 (PE) |       | 48.36.47              | 43.7 | 0.22 (PE) |        |



## 5C PLDR EXPERIMENT

RT = 86.7

Drug = 0.1 mM

cells

0 hr RT 20.000

2hr+RT 10.000 2hr+RT+Drug 10.000 2hr ORT+Drug 200

4hr+RT 5000 4hr+RT+Drug 5000 4hr ORT+Drug 200

6hr+RT 2000 6hr+RT+Drug 2000 6hr ORT+Drug 200

| 5C and Metro toxicity |       |       |       | CHO cells.             |                     |
|-----------------------|-------|-------|-------|------------------------|---------------------|
| $N_2$                 | $O_2$ | $N_2$ | $O_2$ | $5C_1 = 1\text{mM}$    | $M_1 = 20\text{mM}$ |
| $5C_1$                | 3dish | $M_1$ | 3dish | $5C_2 = 0.1\text{mM}$  | $M_2 = 10\text{mM}$ |
| $5C_2$                | "     | $M_2$ | "     | $5C_3 = 0.01\text{mM}$ | $M_3 = 1\text{mM}$  |
| $5C_3$                | "     | $M_3$ | "     |                        |                     |

Plated cell in dish. each dish put 200 cells in incubator 3hr then add drug pump 1hr. after pump. put waterbath 37°C 1hr. then wash off the drug. add new medium. incubator 8 days. then stain. count

Drug: 5C from corner

$136\text{mg} + 40\text{ml} = 1\text{mM}$  each dish add 2.5ml  $136\text{mg} + 40\text{ml} = 20\text{mM}$

$136\text{mg} + 18\text{ml} = 0.1\text{mM}$

$136\text{mg} + 18\text{ml} = 0.01\text{mM}$

Drug: Metro:  $136\text{mg} = 0.136\text{g}$

$136\text{mg} + 40\text{ml} = 20\text{mM}$   
(HBSS)

$136\text{mg} + 4\text{ml} = 10\text{mM}$

$136\text{mg} + 0.4\text{ml} = 1\text{mM}$

|        | $N_2$ Count   | mean  | SF   | $SF/O_2$ |               | $O_2$ Count | mean | SF    | $SF/O_2$ |
|--------|---------------|-------|------|----------|---------------|-------------|------|-------|----------|
| $5C_1$ | 0             |       |      |          | 0             |             |      |       |          |
| $5C_2$ | 129. 108. 104 | 113.7 | 0.57 | 0.848    | 121. 134. 140 | 131.7       | 0.66 | 1.062 |          |
| $5C_3$ | 147. 121. 109 | 125.7 | 0.63 | 0.938    | 129. 138. 117 | 128         | 0.60 | 1.032 |          |
| 0      | 142. 129. 131 | 134   | 0.67 | (CPE)    | 143. 118. 112 | 124.3       | 0.62 | (PE)  |          |
| $M_1$  | 122. 134. 129 | 128.3 | 0.60 | 0.958    | 136. 130. 128 | 129.3       | 0.65 | 1.043 |          |
| $M_2$  | 130. 125. 127 | 127.3 | 0.64 | 0.950    | 130. 124. 120 | 124.7       | 0.62 | 1.005 |          |
| $M_3$  | 133. 130. 119 | 127.3 | 0.64 | 0.950    | 120. 126. 109 | 118.3       | 0.59 | 0.954 |          |

## 5C PLDR Experiment

SC = 0.1 mM

2lw RT 2000

RT = 868

0 Control 200

2lw RT 5000

2lw RT+D 5000 -

2lw D 200

4lw RT 5000

4lw RT+D 5000

4lw D 200

6lw RT 2000

6lw RT+D 2000

6lw D 200

50)

## Nitro-phenyl-Tetrazol (TNB) + Radiation (CHO cell)

Drug =  $10^{-7}$  M

| RT<br>(67°) | N <sub>2</sub> +D | N <sub>2</sub> | RT<br>(67°) | O <sub>2</sub> +D | O <sub>2</sub> |
|-------------|-------------------|----------------|-------------|-------------------|----------------|
| 18          | 20.000            | 10.000         | 8           | 10.000            | 5000           |
| 12          | 2000              | 1000           | 6           | 5000              | 1000           |
| 6           | 1000              | 500            | 4           | 2000              | 500            |
| 0           | 200               | 200            | 0           | 200               | 200            |

Plated cell in dish incubator 3 hr. then add drug pump 1 hr. after post waterbath 37°C 1 hr. then radiation ofic in incubator.

$$\text{Drug from TNB } 10^{-3} \text{ (1MM)} \rightarrow 0.02 \text{ ml} + 1.98 \text{ ml} = 10^{-5}$$

$$1 \text{ ml} + 9 \text{ ml} = 10^{-6}$$

$$8 \text{ ml} + 72 \text{ ml} = 10^{-7}$$

| N <sub>2</sub> +D Count | mean  | SF                   | SF/PE  | N <sub>2</sub> Count | mean  | SF        | SF/PE  |
|-------------------------|-------|----------------------|--------|----------------------|-------|-----------|--------|
| 1. 139. 95. 99          | 111   | 0.0056               | 0.0135 | 64. 78. 36           | 59.3  | 0.0059    | 0.0138 |
| 126. 105. 110. 110      | 108.3 | 0.054                | 0.13   | 84. 26. 52           | 54    | 0.054     | 0.13   |
| 66. 134. 164. 155       | 151   | 0.151                | 0.368  | 72. 71. 60           | 67.7  | 0.135     | 0.31   |
| 0 95. 97. 54            | 82    | 0.41 (PE)            |        | 110. 94. 55          | 86.3  | 0.43 (PE) |        |
| O <sub>2</sub> +D Count |       | O <sub>2</sub> Count |        |                      |       |           |        |
| 86. 74. 80. 73          | 52.3  | 0.005                | 0.009  | 42. 59. 61           | 54    | 0.0108    | 0.018  |
| 61. 148. 135. 130       | 137.7 | 0.028                | 0.0487 | 37. 54. 33           | 41.3  | 0.041     | 0.07   |
| 46. 171. 157. 182       | 170   | 0.085                | 0.15   | 64. 80. 78           | 74    | 0.148     | 0.25   |
| 0 112. 110. 117         | 113   | 0.565 (PE)           |        | 109. 120. 126        | 118.3 | 0.59 (PE) |        |

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5C PLDR Experiment

Drug = 0.1 mM  
RT = 86.7

## Metro + Radiation

Drug = 0.5 mM.

| RT<br>(hr) | N <sub>2</sub> +D | N <sub>2</sub> | RT<br>(hr) | O <sub>2</sub> +D | O <sub>2</sub> |
|------------|-------------------|----------------|------------|-------------------|----------------|
| 18         | 20.000            | 10.000         | 8          | 10.000            | 5000           |
| 12         | 2000              | 1000           | 6          | 2000              | 1000           |
| 6          | 500               | 200            | 4          | 1000              | 200            |
| 0          | 200               | 200            | 0          | 200               | 200            |

plated cells in dish incubator 3 hr then add drug pump 1 hr. then waterbath 37°C 1 hr. then radiation.oxic in incubator. after radiation wash off the drug. add new medium incubator 8 hr.

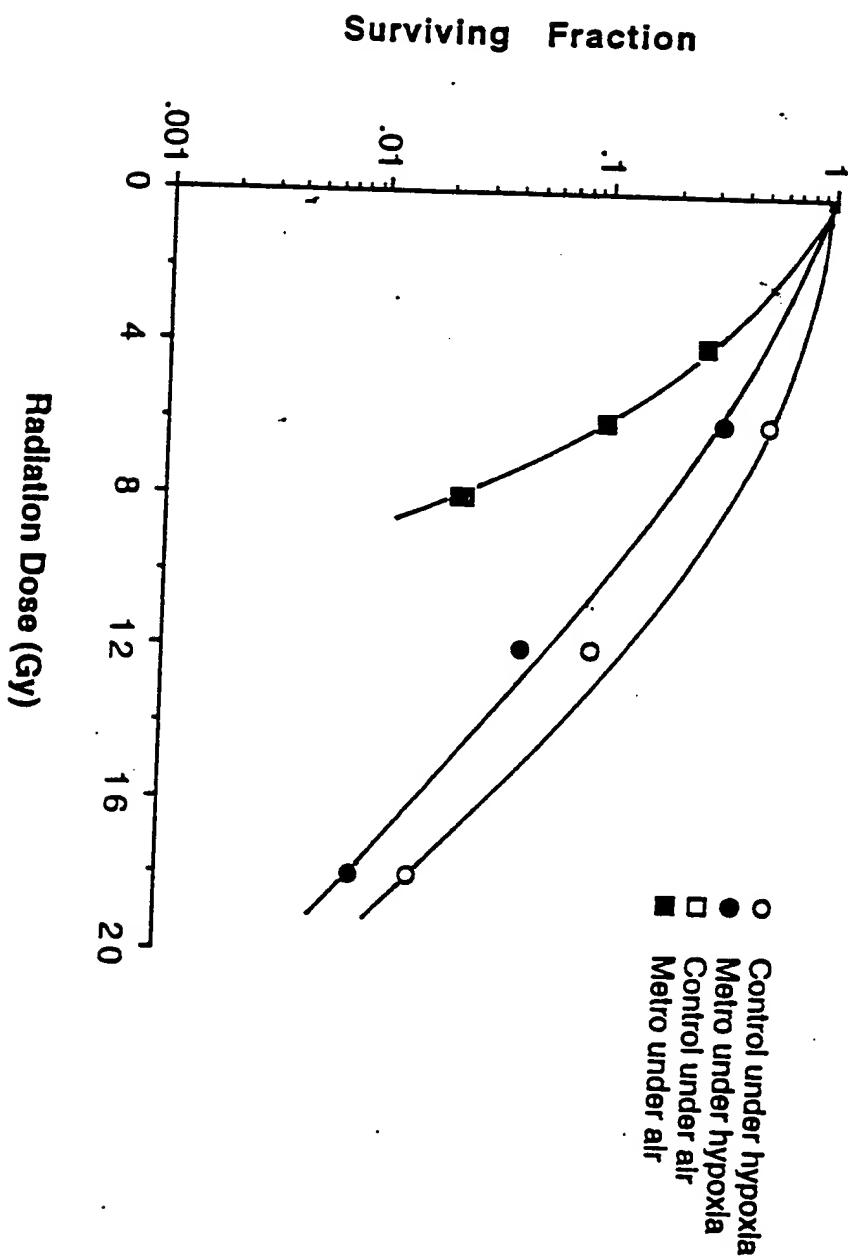
Drug: mortar. 6.84 mg/80 ml (HSS) pack dish 3 ml drug.

| N <sub>2</sub> +D Count    | mean | SE        | SE/PE | N <sub>2</sub> Count | mean | SE        | SE/PE |
|----------------------------|------|-----------|-------|----------------------|------|-----------|-------|
| 18 <sup>1/2</sup> 45.60.46 | 67   | 0.0034    | 0.008 | 64.83.52             | 66.3 | 0.0066    | 0.015 |
| 1-11. 46.78.41             | 38.3 | 0.019     | 0.045 | 43.66.14             | 41   | 0.041     | 0.093 |
| 66 <sup>1/2</sup> 70.70.74 | 71.3 | 0.143     | 0.332 | 37.54.47             | 46   | 0.23      | 0.523 |
| 0 84. 46.80                | 86.7 | 0.43 (PE) |       | 80. 83.10            | 88   | 0.44 (PE) |       |

O<sub>2</sub>+D Count

| O <sub>2</sub> +D Count         | mean  | SE         | SE/PE | O <sub>2</sub> Count | mean  | SE        | SE/PE |
|---------------------------------|-------|------------|-------|----------------------|-------|-----------|-------|
| 86 <sup>1/2</sup> 115. 124.123  | 120.7 | 0.012      | 0.023 | 82.68.59             | 69.7  | 0.014     | 0.024 |
| 66 <sup>1/2</sup> 108. 108. 104 | 106.7 | 0.053      | 0.1   | 57.63.55             | 58.3  | 0.058     | 0.102 |
| 46 <sup>1/2</sup> 137. 150. 152 | 146.3 | 0.146      | 0.274 | 42.20.32             | 31.3  | 0.157     | 0.275 |
| 0 103. 112. 106                 | 107   | 0.535 (PE) |       | 118.106.119          | 114.3 | 0.57 (PE) |       |

55  
Radiosensitizing Effects of Metronidazole (0.5 mM) on CHO Cells



## Metro + Radiation (2nd)

Drug = 0.5 mM

| RT<br>(day) | N <sub>2</sub> +D | N <sub>2</sub> | RT<br>(day) | O <sub>2</sub> +D | O <sub>2</sub> |
|-------------|-------------------|----------------|-------------|-------------------|----------------|
| 18          | 20.000            | 10.000         | 8           | 10.000            | 5000           |
| 12          | 2000              | 1000           | 6           | 2000              | 1000           |
| 6           | 500               | 200            | 4           | 1000              | 200            |
| 0           | 200               | 200            | 2           | 200               | 200            |

plate cell in dish incubated 3 hr then add drug pump 1 hr. after pump put water bath 37°C 1 hr. then radiation. ofic work in incubator. after radiation wash off the drug. add new medium incubator 7 day stain.

Drug: Metro 6.8 ng/10ml HBSS.

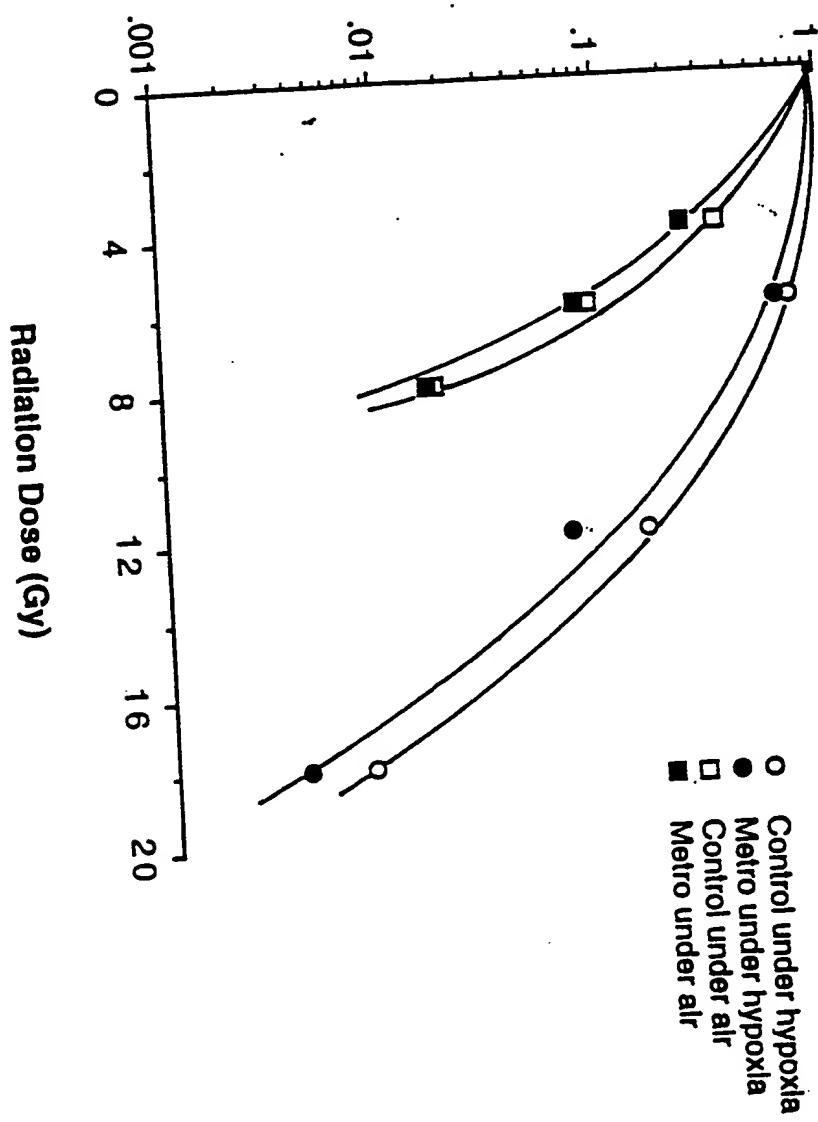
|     | N <sub>2</sub> +D Count | mean  | SF        | SF/PE | N <sub>2</sub> Count | mean | SF        | SF/PE |
|-----|-------------------------|-------|-----------|-------|----------------------|------|-----------|-------|
| 186 | 34.32.32                | 32.7  | 0.0016    | 0.004 | 37.46.26             | 36.3 | 0.0036    | 0.008 |
| 126 | 49.50.65                | 54.7  | 0.027     | 0.064 | 66.67.60             | 64.3 | 0.064     | 0.147 |
| 66  | 123.122.120             | 121.7 | 0.243     | 0.611 | 43.84.56             | 61   | 0.305     | 0.698 |
| 0   | 57.48.84                | 79.7  | 0.398(PE) |       | 70.79.113            | 87.3 | 0.437(PE) |       |

|    | O <sub>2</sub> +D Count | O <sub>2</sub> Count |
|----|-------------------------|----------------------|
| 86 | 132.134.102             | 122.7                |
| 66 | 104.124.115             | 114.3                |
| 46 | 187.204.149             | 180                  |
| 0  | 141.138.171             | 150                  |

37°C  
37°C

Surviving Fraction  
(2nd)

**Radiosensitizing Effects of Metronidazole (0.5mM) on CHO Cells**



[REDACTED] Tarol on CHO cells (2 hr treatment 28 hr later trypsinized experiment)

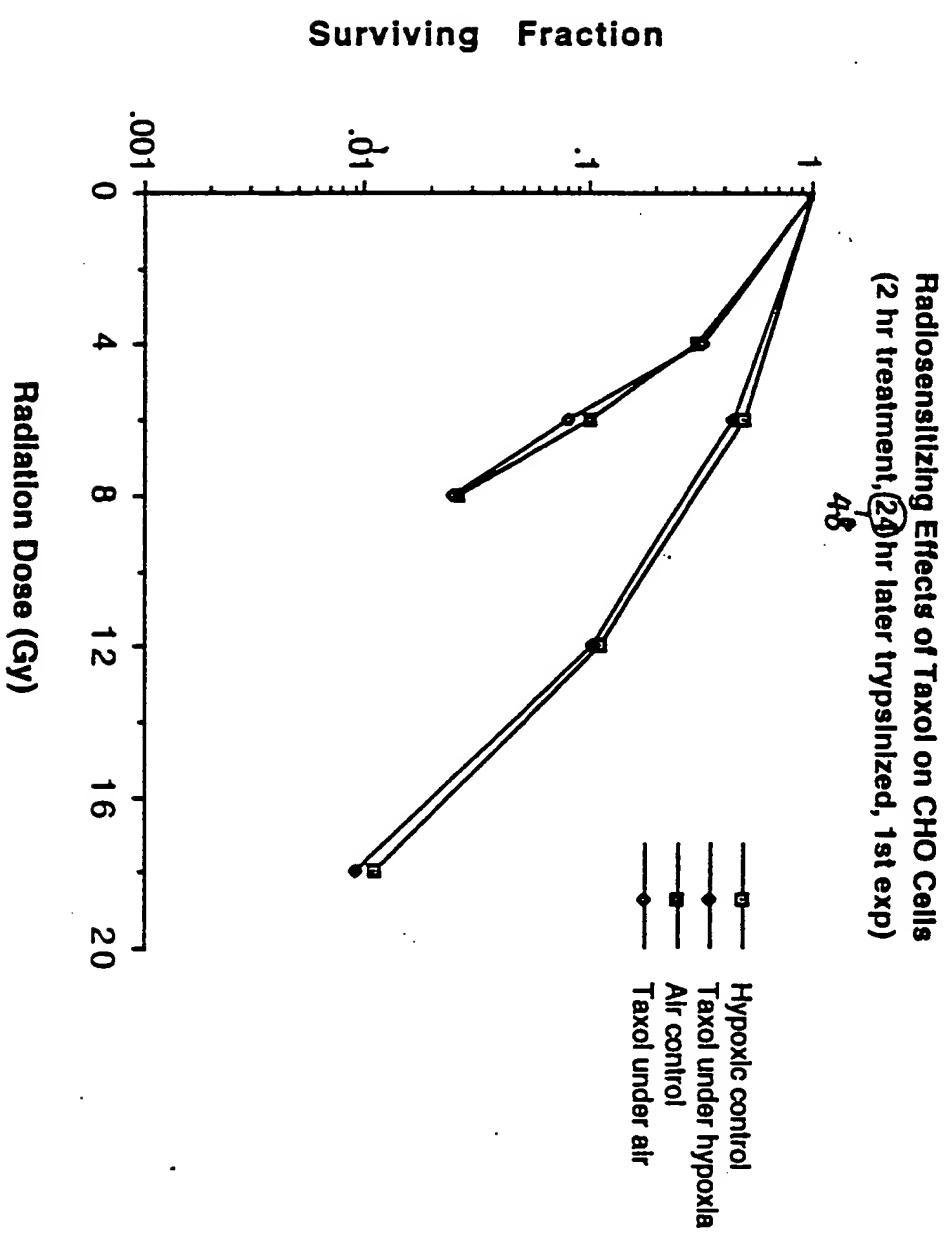
plant cell in 2 dishes (cover glass)  $5 \times 10^4$ . one day later one dish add  $5 \times 10^{-6}$  ml Tarol with HBSS. one dish add HBSS with DMSO 2 hr at  $37^\circ\text{C}$  incubator then wash off the dish put new medium incubator 28 hrs. then trypsinize then plant cells in dish incubator later 2 hours. then hypoxic 1 hr at 25°C incubator. then irradiate after radiation put in incubator 7 days later stain. Count

|   | $N_2 + \text{Tarol}$ | $N_2 + \text{HBSS}$ | $O_2 + \text{Tarol}$ | $O_2 + \text{HBSS}$ | diff: from $10^{-3}$ (1 mM) |
|---|----------------------|---------------------|----------------------|---------------------|-----------------------------|
| - | 18                   | 10,000              | 10,000               | 8                   | 2000                        |
| - | 12                   | 2000                | 2000                 | 6                   | 1000                        |
| - | 6                    | 500                 | 500                  | 4                   | 500                         |
| - | 0                    | 200                 | 200                  | 0                   | 200                         |

|   | $N_2 + D$ Count | mean        | SF    | SF/PE | $N_2 + H_2S$ Count | mean        | SF    | SF/PE |       |
|---|-----------------|-------------|-------|-------|--------------------|-------------|-------|-------|-------|
| - | 1869            | 61.45.71    | 59    | 0.059 | 0.059              | 73.87.92    | 84    | 0.084 | 0.11  |
| - | 1209            | 124.159.115 | 132.7 | 0.066 | 0.104              | 165.186.172 | 174.3 | 0.087 | 0.113 |
| - | 609             | 150.134.130 | 138   | 0.276 | 0.435              | 174.191.193 | 186   | 0.372 | 0.482 |
| - | 0               | 137.120.124 | 127   | 0.635 | (PE)               | 160.156.147 | 154.3 | 0.772 | (PE)  |

$O_2 + H_2S$  Count

|     |          |             |       |       |             |             |       |       |      |
|-----|----------|-------------|-------|-------|-------------|-------------|-------|-------|------|
| 864 | 30.35.20 | 28.3        | 0.014 | 0.025 | 40.44.41    | 41.7        | 0.021 | 0.026 |      |
| 604 | 62.36.39 | 45.7        | 0.046 | 0.08  | 89.74.75    | 79.3        | 0.079 | 0.1   |      |
| 464 | 83.92.98 | 91          | 0.182 | 0.318 | 116.117.124 | 119.        | 0.238 | 0.301 |      |
| -   | 0        | 114.114.116 | 114.7 | 0.573 | (PE)        | 160.161.153 | 158   | 0.79  | (PE) |



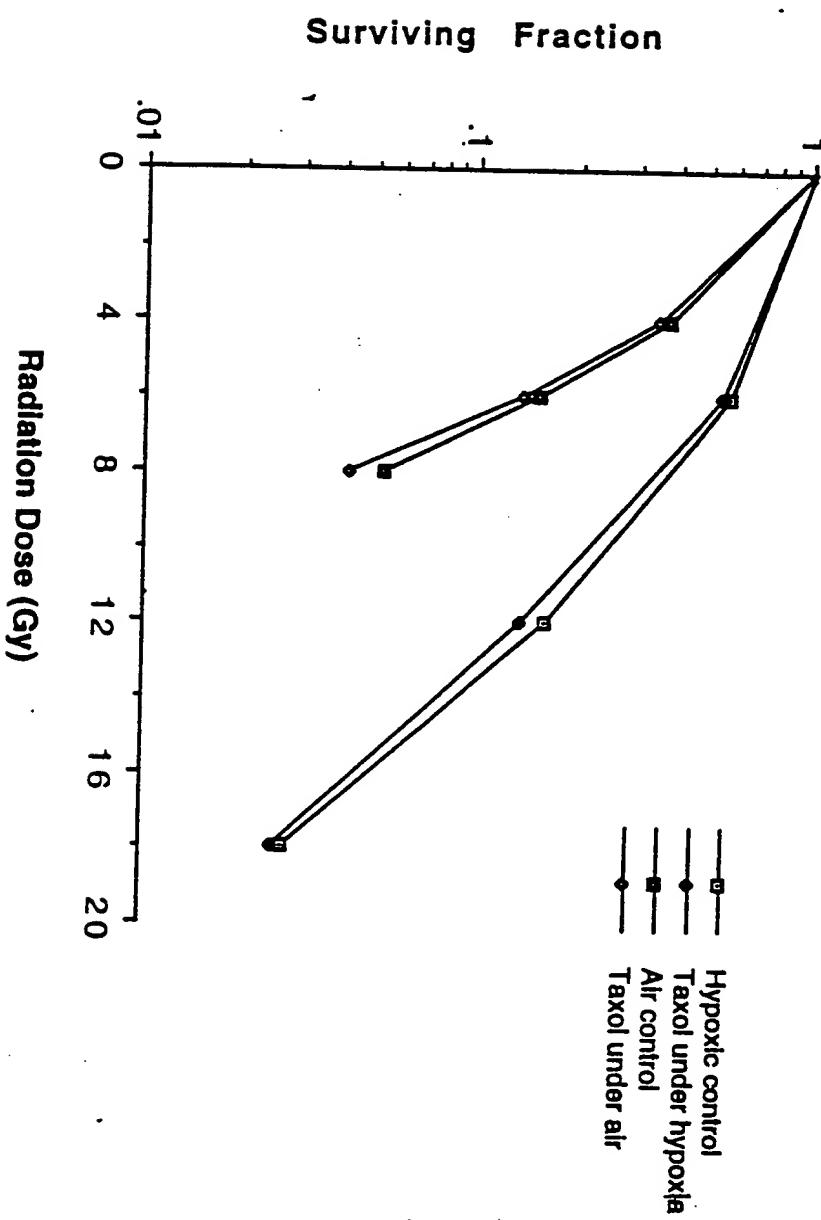
61)

Tabel on CHO cells (2 hr treatment 48 hr later trypsinized Experiment 2)

Report [REDACTED] Experiment

| RT<br>(hr)                       | N <sub>2</sub> +D | N <sub>2</sub> +HBSS       | RT<br>(hr) C <sub>2</sub> +D | O <sub>2</sub> +HBSS       | drop from total<br>$\times 10^{-3}$ (mm) |
|----------------------------------|-------------------|----------------------------|------------------------------|----------------------------|--|
| 18                               | 10.000            | 10.000                     | 8 2000                       | 2000                       |  |
| 12                               | 2000              | 2000                       | 6 1000                       | 1000                       | 1.05 ml + 4.15 ml = 5.10 ml<br>(HBSS)    |
| 6                                | 500               | 500                        | 4 500                        | 500                        | 6.05 ml + 9.95 ml<br>DMSO HBSS           |
| 0                                | 200               | 200                        | 0 200                        | 200                        |  |
| <i>N<sub>2</sub>+Tabel Count</i> |                   | mean                       | SF SF/PE                     | <i>N<sub>2</sub> Count</i> | mean SF SF/PE                            |
| 18 <sup>64</sup>                 | 112. 125. 87      | 108                        | 0.018 0.025                  | 168. 186. 159              | 171 0.0171 0.027                         |
| 12 <sup>64</sup>                 | 127. 119. 107     | 117.7                      | 0.059 0.137                  | 197. 209. 210              | 205.3 0.103 0.161                        |
| 6 <sup>64</sup>                  | 124. 108. 112     | 114.7                      | 0.229 0.533                  | 187. 173. 183              | 181 0.362 0.568                          |
| 0                                | 77. 88. 94        | 86.3                       | 0.43 (PE)                    | 115. 122. 145              | 127.3 0.637 (PE)                         |
| <i>C<sub>2</sub>+D Count</i>     |                   | <i>O<sub>2</sub> Count</i> |                              |                            |  |
| 8 <sup>64</sup>                  | 33. 34. 41        | 36                         | 0.018 0.041                  | 78. 82. 52                 | 70.7 0.035 0.052                         |
| 6 <sup>64</sup>                  | 59. 58. 65        | 60.7                       | 0.061 0.138                  | 106. 103. 99               | 102.7 0.103 0.152                        |
| 4 <sup>64</sup>                  | 68. 75. 83        | 75.3                       | 0.151 0.342                  | 117. 132. 127              | 125.3 0.251 0.371                        |
| 0                                | 88. 86. 92        | 88.7                       | 0.04 (PE)                    | 126. 141. 138              | 135 0.675 (PE)                           |

Radiosensitizing Effects of Taxol on CHO Cells  
(2 hr treatment, 48 hr later trypsinized, 2nd exp)



Total: T-B on HCT cells toxicity  
 $\bar{O}_2$  count mean

T-5 3 dishes 0.22

T-6 " 0

T-7 " 0

T-8 " 2.00

T-B-5 " 0.00

T-B-6 " 0.00

T-B-7 " 0.00

T-B-8 " 1.00

0 69.66.62 65.7 0.308 (PE)

plant cell in dish incubator. For  $\bar{O}_2$  then add drug incubator 24 hrs. then wash off  
 the drug. put new medium <sup>help in incubator</sup> ~~10% FBS~~ stain

Drug Total: from  $10^3$  (cm<sup>2</sup>)

$$0.18 \text{ ml} + 2.39 \text{ ml} = 7 \times 10^{-5} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-5}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 7 \times 10^{-6} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-6}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 7 \times 10^{-7} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-7}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 7 \times 10^{-8} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-8}$$

T-B from  $10^3$  (cm<sup>2</sup>)

$$0.18 + 2.39 \text{ ml} = 7 \times 10^{-5} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-5}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 7 \times 10^{-6} \text{ each dish add } 0.5 \text{ ml} + 3 \text{ ml} = 10^{-6}$$

## Nitro-phenyl-toxol + Radiation on CHO cells

TMB = 10<sup>7</sup>

| RT<br>of | N <sub>2</sub> +D | N <sub>2</sub> | RT<br>(C <sub>2</sub> ) C <sub>2</sub> +D | O <sub>2</sub> |
|----------|-------------------|----------------|---|----------------|
| 18       | 20000             | 10000          | 8 5000                                    | 2000           |
| 12       | 5000              | 2000           | 6 2000                                    | 1000           |
| 6        | 1000              | 500            | 4 1000                                    | 500            |
| 0        | 200               | 200            | 0 200                                     | 200            |

plant cell in dish incubator for 6 hrs. then add drug pump 1 hr. after pump with chamber put incubator <sup>for</sup> 24 hrs. then irradiate after radiation wash off the drug put new medium. incubator 7 days stain

$$\text{Drug} = TMB \text{ fmM} \rightarrow 0.02 \text{ ml} + 1.98 \text{ ml} = 10^{-5}$$

$$1 \text{ ml} + 9 \text{ ml} = 10^{-6}$$

$$1 \text{ ml} + 9 \text{ ml} = 10^{-7}$$

|    | N <sub>2</sub> +D Count | mean  | SF     | SF/PE  | N <sub>2</sub> Count | mean  | SF     | SF/PE  |
|----|-------------------------|-------|--------|--------|----------------------|-------|--------|--------|
| 18 | 88.89.83                | 86.7  | 0.004  | 0.0088 | 81.78.70             | 76.3  | 0.0076 | 0.0141 |
| 12 | 206. 177. 207           | 196.7 | 0.039  | 0.08   | 147. 102. 172.       | 153.7 | 0.077  | 0.142  |
| 6  | 243. 205. 199           | 229   | 0.229  | 0.467  | 205. 190. 172        | 189   | 0.378  | 0.7    |
| 0  | 109. 100. 85            | 98    | 0.49   | (PE)   | 102. 123. 101        | 108.7 | 0.54   | (PE)   |
|    | O <sub>2</sub> +D Count |       |        |        | O <sub>2</sub> Count |       |        |        |
| 8  | 51. 50. 74              | 58.3  | 0.012  | 0.046  | 125. 123. 123        | 123.7 | 0.062  | 0.097  |
| 6  | 60. 70. 73              | 67.7  | 0.0338 | 0.133  | 196. 210. 207        | 204.3 | 0.204  | 0.321  |
| 4  | 70. 74. 79              | 74.3  | 0.074  | 0.293  | 183. 192. 191        | 188.7 | 0.377  | 0.592  |
| 0  | 53. 47. 53              | 51    | 0.255  | (PE)   | 132. 118. 132        | 127.3 | 0.637  | (PE)   |

## Taxol and Taxol-B Toxicity on HCT cells.

| T=Taxol      | Plant cell Count | Taxol-B. planted's Count |
|--------------|------------------|--------------------------|
| $T-10^{-6}$  | 500              | 0                        |
| $T-10^{-7}$  | 500              | 1.00                     |
| $T-10^{-8}$  | 500              | 2.31                     |
| $T-10^{-9}$  | 500              | 0.00                     |
| $T-10^{-10}$ | 500              | 5.02                     |

| T-B- $10^{-6}$ | 500 | 0    |
|----------------|-----|------|
| $T-B-10^{-7}$  | 500 | 1.00 |
| $T-B-10^{-8}$  | 500 | 0.01 |
| $T-B-10^{-9}$  | 500 | 1.11 |
| $T-B-10^{-10}$ | 500 | 1.21 |

Control: 200 150-150.152

plant HCT cells in dish, each dish 500 cells. control 200 cells. incubator 5.5 hr later add 0.5 ml drug. total 3.5 ml each dish drug in medium. then keep incubator 24 hrs. with drug. later wash off the drug. add new medium keep incubator for 9 days. stain.

Dilution: from: Taxol . Taxol-B.  $10^{-3}$  (1ml)

$$0.12 \text{ ml} + 1.88 \text{ ml} = 2 \times 10^{-5}$$

$$0.18 \text{ ml} + 2.32 \text{ ml} = 2 \times 10^{-5}$$

$$0.24 \text{ ml} + 1.8 \text{ ml} = 2 \times 10^{-6}$$

$$0.24 \text{ ml} + 1.8 \text{ ml} = 2 \times 10^{-7}$$

$$0.24 \text{ ml} + 1.8 \text{ ml} = 2 \times 10^{-8}$$

$$0.24 \text{ ml} + 1.8 \text{ ml} = 2 \times 10^{-9}$$

$$0.24 \text{ ml} + 1.8 \text{ ml} = 2 \times 10^{-10}$$

each dish add 0.5 ml with dish medium 3 ml. total 3.5 ml

(drug)

 $= 10^{-6}$

## T-M and TNB in HCT cell toxicity

| T-M            | conc | Count       | mean  | SF    | SF/PE |
|----------------|------|-------------|-------|-------|-------|
| T-M $10^{-7}$  | 500  | 0           | 0     |       |       |
| T-M $10^{-8}$  | 500  | 10.4.6      | 6.7   | 0.073 | 0.019 |
| T-M $10^{-9}$  | 500  | 212.235.197 | 214.7 | 0.429 | 0.609 |
| T-M $10^{-10}$ | 500  | 221.222.243 | 228.7 | 0.457 | 0.649 |
| TNB $10^{-7}$  | 500  | 0 0 0       |       |       |       |
| TNB $10^{-8}$  | 500  | 7.5.6       | 6     | 0.012 | 0.017 |
| TNB $10^{-9}$  | 500  | 174.215.160 | 183   | 0.366 | 0.519 |
| TNB $10^{-10}$ | 500  | 187.189.178 | 184.7 | 0.369 | 0.524 |
|                | 200  | 121.143.159 | 141   | 0.705 | (PE)  |

plant 500 HCT cells each dish in incubator for 6hr. then add drug with medium  
keep in incubator 24 hrs. later wash off the drug. add new medium incubator keep for  
4 days stain.

Drug from  $10^{-3}$  (1mM)

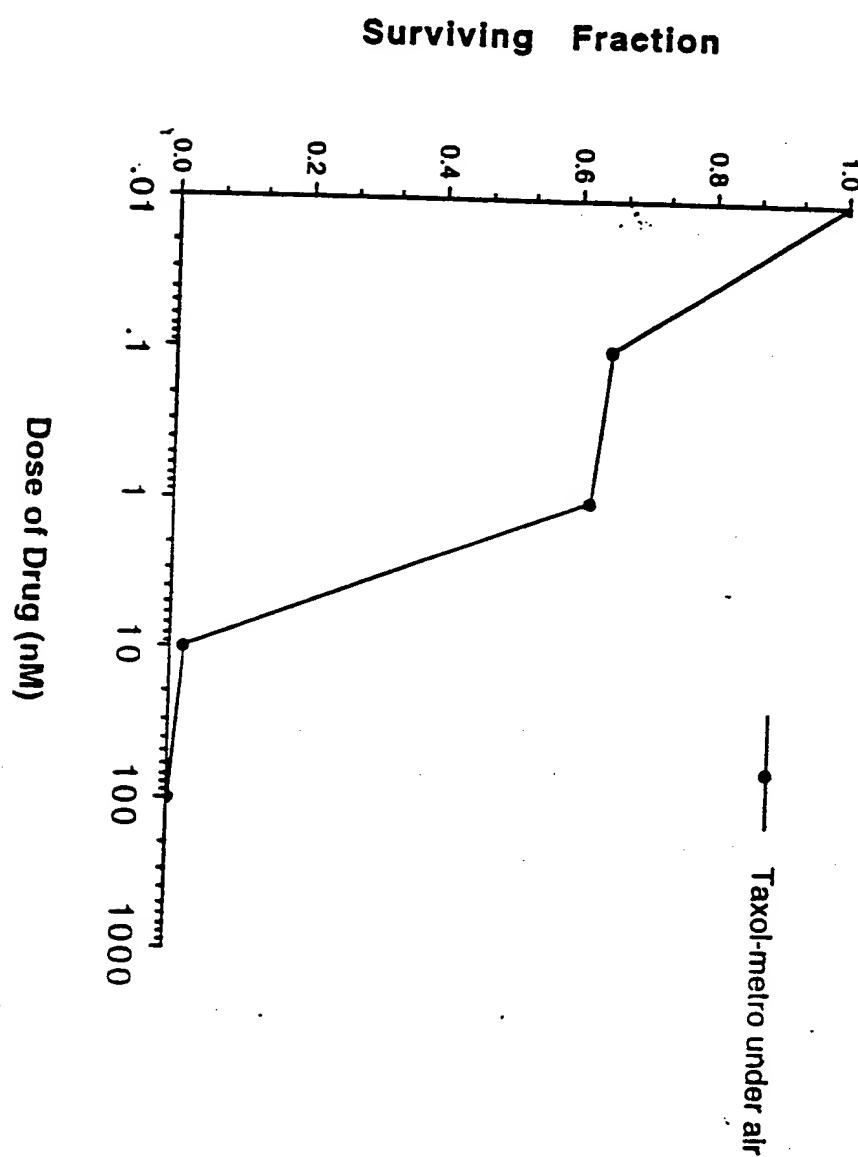
$$11 \text{ ml} + 9.98 \text{ ml} = 1.1 \times 10^{-6} \rightarrow \text{each dish add } \frac{0.3 \text{ ml} + 3 \text{ ml}}{(\text{drug})} = 10^{-7} \text{ (old medium)}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 1.1 \times 10^{-7}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 1.1 \times 10^{-8}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 1.1 \times 10^{-9}$$

Ch moth rap ulic Activities of  
Taxol-metro against HCT Cancer Cells



71)

## Taxol-Metro + Radiation (Repeat Experiment)

 $D = 10^{-7}$ 

| RT   | N <sub>2</sub> +D | N <sub>2</sub> | O <sub>2</sub> +D | O <sub>2</sub> |
|------|-------------------|----------------|-------------------|----------------|
| 180f | 20.000            | 10.000         | 80f 5000          | 2000           |
| 120f | 2000              | 2000           | 60f 2000          | 500            |
| 60f  | 500               | 500            | 40f 1000          | 200            |
| 0    | 200               | 200            | 0                 | 200            |

plant CHO cells in dark incubator for 3 hr. then add drug with HIBSS pump 1 hr. ofic in incubator. after pump, put waterbath 37°C 1 hr. then irradiate. after RT. wash off the drug, add new medium keep incubator 2 days. stain.

Drug: from T-M.  $T = 13 \cdot 10^{-3}$  (1 mM)

$$\frac{1}{2000} \cdot 1.98 \cdot d = 10^{-5}$$

$$\frac{1}{1000} \cdot 1.98 \cdot d = 10^{-6}$$

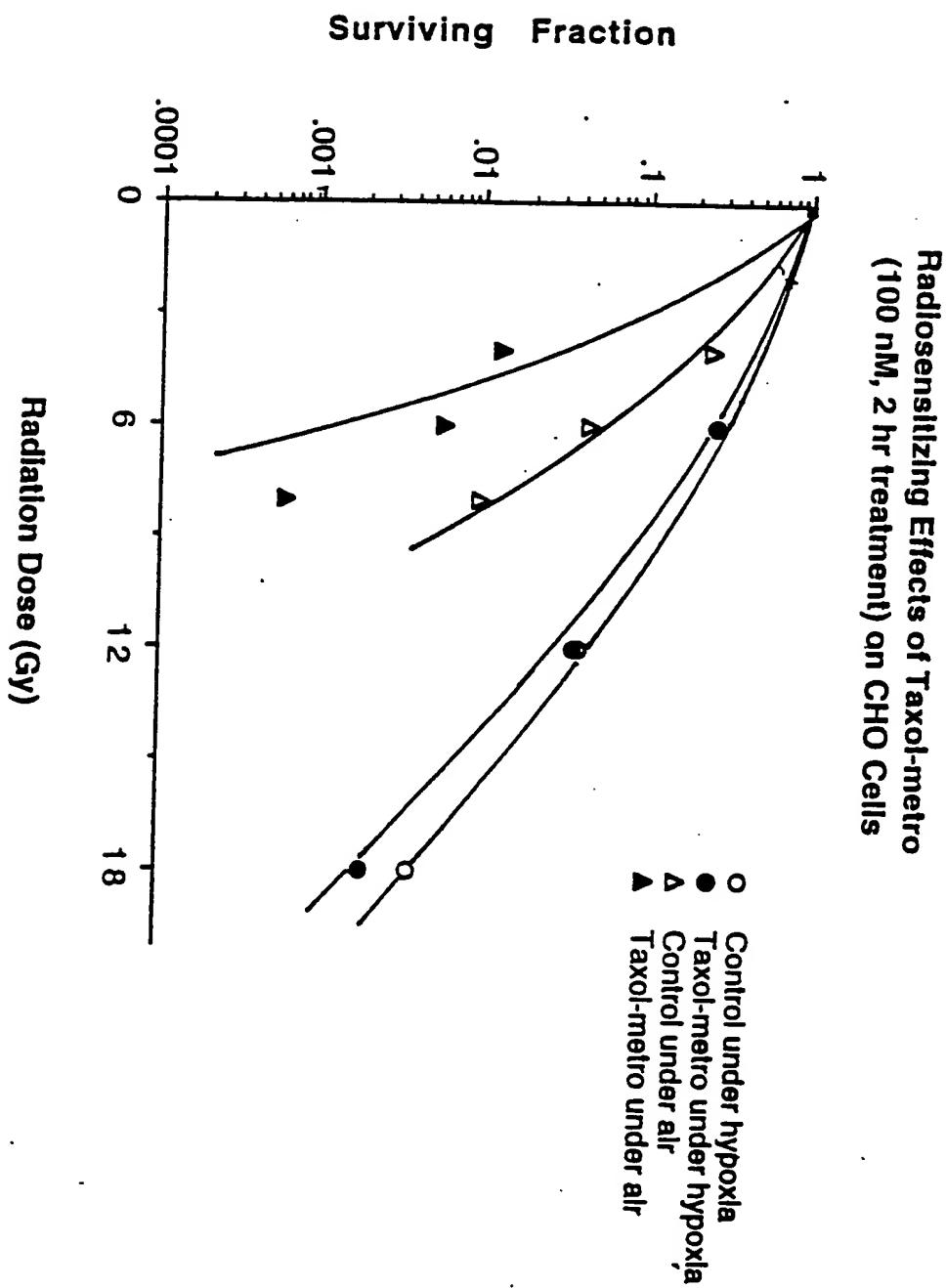
$$0.8 \cdot 1.98 \cdot d = 10^{-7}$$

$$8 \cdot 1.98 \cdot d = 10^{-7}$$

|      | N <sub>2</sub> +D Count | mean  | SF         | SF/PE | N <sub>2</sub> Count | mean  | SF         | SF/PE |
|------|-------------------------|-------|------------|-------|----------------------|-------|------------|-------|
| 180f | 27. 20. 21              | 22.7  | 0.001      | 0.002 | 27. 40. 34           | 24.7  | 0.0025     | 0.004 |
| 120f | 41. 41. 48              | 43.3  | 0.022      | 0.037 | 57. 58. 44           | 53    | 0.0265     | 0.041 |
| 60f  | 84. 88. 62              | 78    | 0.156      | 0.27  | 104. 74. 77          | 85    | 0.17       | 0.264 |
| 0    | 111. 120. 116           | 115.7 | 0.578 (PE) |       | 120. 126. 140        | 128.7 | 0.643 (PE) |       |

O<sub>2</sub>+D Count

|     | O <sub>2</sub> +D Count | mean | SF         | SF/PE         |
|-----|-------------------------|------|------------|---------------|
| 80f | 1. 0. 2                 | 0.3  | 0.0007     | 0.0006        |
| 60f | 1. 1. 2                 | 1.3  | 0.0007     | 0.006         |
| 40f | 1. 1. 2                 | 1.3  | 0.001      | 0.013         |
| 0   | 18. 23. 21              | 20.7 | 0.103 (PE) | 118. 104. 115 |



1000L-Nicotin + Radiation on CHO cells (Repeat [REDACTED] Experiment)

| RTG | Nz+D   | Nz     | RTG+Oz+D | Oz   |
|-----|--------|--------|----------|------|
| 18  | 20.000 | 10.000 | 8 5000   | 2000 |
| 16  | 5000   | 2000   | 6 2000   | 1000 |
| 12  | 1000   | 500    | 4 1000   | 500  |
| 0   | 200    | 200    | 0 200    | 200  |

plant cell in dish incubator for 6 hrs. then add drug with HBSS pump 1 hr. stic in incubator after pump put chamber into incubator for 24 hrs. then take out radiation after RT. wash off the drug add new medium <sup>to</sup> keep in incubator for 8 days <sup>then</sup> stain it.

Drug: from T-M. TNB  $10^{-3}$  (1 mM)

$$2 \text{ ml} + 1.98 \text{ ml} = 10^{-5}$$

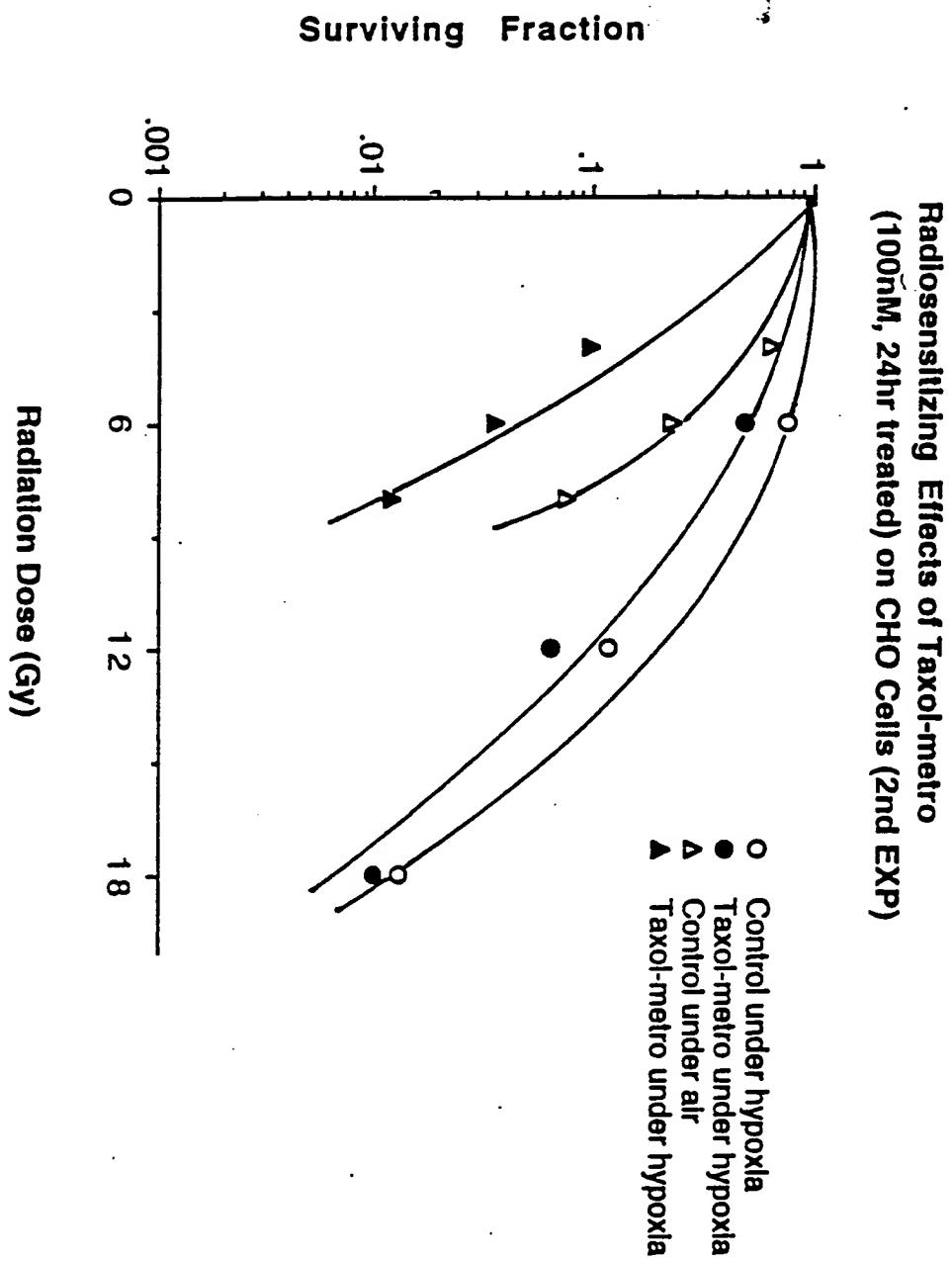
$$0.8 \text{ ml} + 7.2 \text{ ml} = 10^{-6}$$

$$8 \text{ ml} + 72 \text{ ml} = 10^{-7}$$

each dish add 3 ml drug with HBSS.

|      | Nz+D Count  | mean  | SE         | SE/PE  | Nz Count    | mean  | SE         | SE/PE |
|------|-------------|-------|------------|--------|-------------|-------|------------|-------|
| 18Gf | 35.45.55.   | 45    | 0.00275    | 0.0099 | 56.48.31    | 45    | 0.0045     | 0.013 |
| 12Gf | 57.71.91    | 73    | 0.0146     | 0.064  | 86.109.58   | 84.3  | 0.042      | 0.118 |
| 6Gf  | 81.113.137. | 110.3 | 0.11       | 0.484  | 162.128.113 | 134.3 | 0.269      | 0.753 |
| 0    | 37.65.24    | 46.7  | 0.228 (PE) |        | 62.80.72    | 71.3  | 0.357 (PE) |       |

|     | Oz+D Count | mean | SE         | SE/PE | Oz Count    | mean  | SE         | SE/PE |
|-----|------------|------|------------|-------|-------------|-------|------------|-------|
| 8Gf | 2.5.3      | 3.3  | 0.0007     | 0.012 | 101.77.78   | 83.3  | 0.043      | 0.077 |
| 6Gf | 6.3.3      | 4    | 0.002      | 0.036 | 123.125.137 | 128.3 | 0.128      | 0.23  |
| 4Gf | 3.4.9      | 5.3  | 0.005      | 0.097 | 156.190.187 | 177.7 | 0.355      | 0.638 |
| 0   | 16.6.11    | 11   | 0.055 (PE) |       | 124.110.100 | 111.3 | 0.557 (PE) |       |



## TAXOL+RT on HCT cell

$$\text{Drug} = 10^{-9}$$

| RT               | N <sub>2</sub> +D | N <sub>2</sub> | RT              | O <sub>2</sub> +D | O <sub>2</sub> |
|------------------|-------------------|----------------|-----------------|-------------------|----------------|
| 186 <sub>2</sub> | 20.000            | 20.000         | 86 <sub>2</sub> | 20.000            | 20.000         |
| 120 <sub>2</sub> | 10.000            | 10.000         | 66 <sub>2</sub> | 10.000            | 10.000         |
| 60 <sub>2</sub>  | 5000              | 5000           | 46 <sub>2</sub> | 5000              | 5000           |
| 0                | 200               | 200            | 0               | 200               | 200            |

plant HCT cell in dish incubator for 24 hrs. then add drug hypoxic pump 1hr. after pump with chamber put incubator 24 hrs. etc add drug keep in incubator 24 hrs. later X-ray. after X-ray wash off the drug. add new medium keep in incubator 9 days. then stain it. and count

$$\text{Drug - Taxol: from } 10^{-3} \text{ (mm)} \rightarrow 1.1 \text{ ml} + 9.48 \text{ ml (HBSS)} = 1.1 \times 10^{-6}$$

$$0.2 \text{ ml} + 1.8 \text{ ml} = 1.1 \times 10^{-7}$$

$$0.8 \text{ ml} + 7.2 \text{ ml} = 1.1 \times 10^{-8} \text{ each dish add } 0.3 \text{ ml} + 3 \text{ ml (HBSS)} = 10^{-9}$$

| RT               | N <sub>2</sub> +D Count | mean | SF         | S <sup>2</sup> /P <sub>2</sub> | N <sub>2</sub> Count | mean | SF         | S <sup>2</sup> /P <sub>2</sub> |
|------------------|-------------------------|------|------------|--------------------------------|----------------------|------|------------|--------------------------------|
| 186 <sub>2</sub> | 0                       | 0    | 0          | 0                              | 7.8.7                | 7.3  | 0.0037     | 0.00197                        |
| 120 <sub>2</sub> | 3.2.2.                  | 2.3  | 0.0002     | 0.00076                        | 45.43.58             | 48.7 | 0.0097     | 0.0262                         |
| 66 <sub>2</sub>  | 42.35.28                | 35   | 0.007      | 0.0228                         | 74.80.69             | 74.3 | 0.372 (PE) |                                |
| 0                | 70.53.61                | 61.3 | 0.307 (PE) |                                |                      |      |            |                                |

|                 | O <sub>2</sub> +D Count | 12.3 | 0.0006     | 0.0013 | 14.15.20    | 16.3  | 0.00082    | 0.0015 |
|-----------------|-------------------------|------|------------|--------|-------------|-------|------------|--------|
| 36 <sub>2</sub> | 9.14.14                 | 63   | 0.0063     | 0.0132 | 120.97.100  | 105.7 | 0.0106     | 0.019  |
| 60 <sub>2</sub> | 75.60.54                | 195  | 0.039      | 0.082  | 278.281.249 | 289.3 | 0.054      | 0.097  |
| 60 <sub>2</sub> | 200.187.198             | 45.3 | 0.477 (PE) |        | 17.107.108  | 110.7 | 0.553 (PE) |        |
| 0               | 45.79.112               |      |            |        |             |       |            |        |

Tarol-Tarol-t-bu, Tarol-Metro, Nitrophenyl-Tarol on HCT cells under air toxicity

| Tarol                     | Count      | mean  | SE         | SE/PE  |
|---------------------------|------------|-------|------------|--------|
| T $2 \times 10^{-8}$      | 1.0.0      | 0.5   | 0.0025     | 0.0046 |
| T $4 \times 10^{-9}$      | 4.1.1      | 2     | 0.001      | 0.0185 |
| T $8 \times 10^{-10}$     | 81.74.76   | 77    | 0.385      | 0.71   |
| T $1.6 \times 10^{-10}$   | 107.11.118 | 112   | 0.56       | 1.0332 |
| Tarol-t-bu                |            |       |            |        |
| T-B $2 \times 10^{-8}$    | 1.3        | 2     | 0.01       | 0.0185 |
| T-B $4 \times 10^{-9}$    | 0.1.0      | 0.33  | 0.007      | 0.0031 |
| T-B $8 \times 10^{-10}$   | 2.2.1      | 1.667 | 0.0083     | 0.0154 |
| T $1.6 \times 10^{-10}$   | 43.35.35   | 37.7  | 0.1883     | 0.3425 |
| Tarol-Metro               | *          |       |            |        |
| T-M $2 \times 10^{-8}$    | 0.0.0      | 0     |            |        |
| T-M $4 \times 10^{-9}$    | 1.2.1      | 1.33  | 0.007      | 0.0123 |
| T-M $8 \times 10^{-10}$   | 2.4.4      | 3.3   | 0.07       | 0.031  |
| T-M $1.6 \times 10^{-10}$ | 0.2.1      | 1     | 0.005      | 0.0092 |
| TNB $2 \times 10^{-8}$    | 0.0.0      | 0     | 0          | 0      |
| TNB $4 \times 10^{-9}$    | 0.0.1      | 0.3   | 0.0017     | 0.0051 |
| TNB $8 \times 10^{-10}$   | 0.1.1      | 0.667 | 0.003      | 0.0062 |
| TNB $1.6 \times 10^{-10}$ | 2.1.1      | 1.33  | 0.007      | 0.0123 |
| Control                   | 100.11.114 | 108.3 | 0.542 (PE) |        |

plant HCT cells in dish incubator 6hr. then add drug with medium keep in incubator for 24hrs. then wash off the drug. add new medium incubator for 9days. stain.

Drug: T, T-B, T-M, TNB from  $10^{-3}$  (1mM)

$$25\text{ml} + 2.475 = 10^{-5}$$

$$0.5\text{ml} + 4.5\text{ml} = 10^{-6}$$

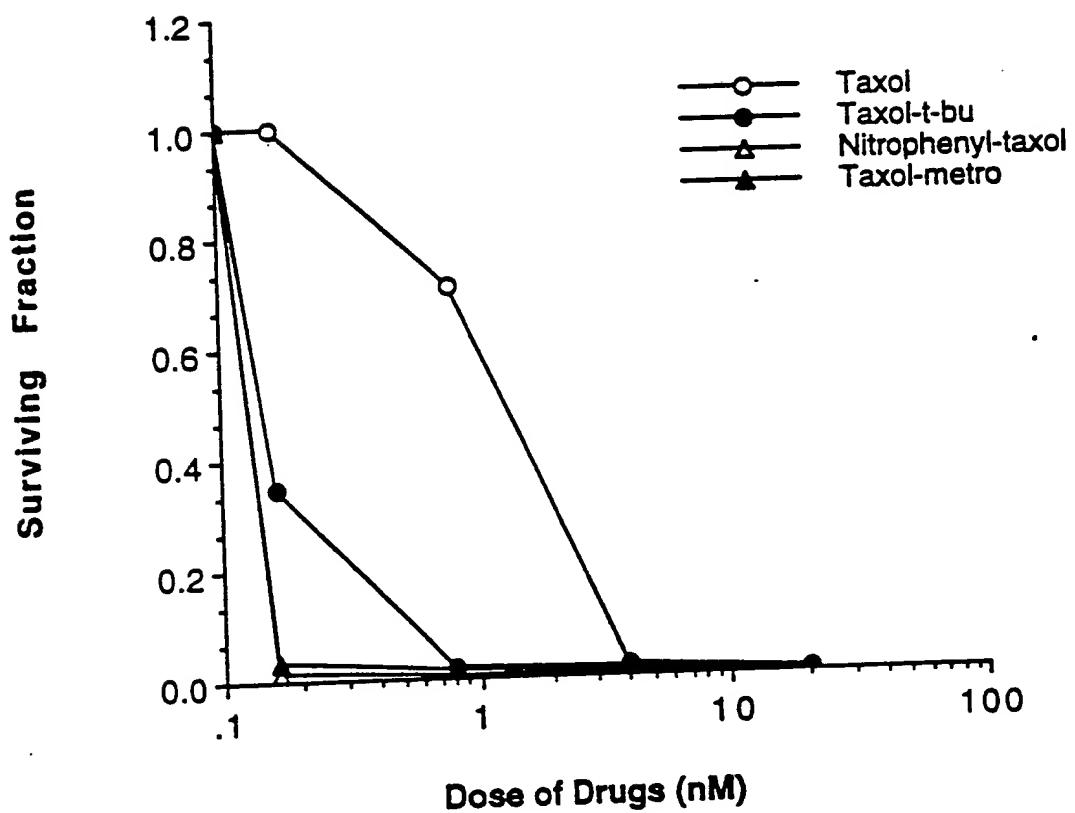
$$0.5\text{ml} + 4.5\text{ml} = 10^{-7}$$

$$3\text{ml} + 12\text{ml} = 4 \times 10^{-9}$$

$$3\text{ml} + 12\text{ml} = 8 \times 10^{-8}$$

$$3\text{ml} + 12\text{ml} = 1.6 \times 10^{-10}$$

Chemotherapeutic activities of Taxol, Taxol-t-bu,  
Nitrophenyl-taxol, and Taxol-metro on HCT116 Cells  
under air condition (1st exp)



115  
T-B on HCT cell + Radiation

$T-B = 5 \times 10^8$

| RTGf | N <sub>2</sub> +D | N <sub>2</sub> | RTGf | D <sub>2</sub> +D | O <sub>2</sub> |
|------|-------------------|----------------|------|-------------------|----------------|
| 18   | 40000             | 40000          | 8    | 40000             | 40000          |
| 12   | 20.000            | 20.000         | 6    | 10.000            | 10.000         |
| 6    | 5000              | 5000           | 4    | 2000              | 2000           |
| 0    | 200               | 200            | 6    | 200               | 200            |

plant HCT cells in dish incubated for 6 hrs. then add drug pump 1 hr. at 37°C in incubator. after pump, put incubator 23 hrs. total with drug for 24 hrs. then radiation. later wash off the drug. add new medium incubator for 9 days. then stain. count.

Drug. from T-B ( $10^{-3}$  (1mm))

$$0.4 \text{ ml} + 3.6 \text{ ml} (TBS) = 1.1 \times 10^{-6}$$

$$0.4 + 3.6 \text{ ml} = 1.1 \times 10^{-7}$$

$$4 \text{ ml} + 4 \text{ ml} = 5.5 \times 10^{-8} \quad \text{each dish add } 0.3 \text{ ml} + 3 \text{ ml} = 5 \times 10^{-9}$$

|      | N <sub>2</sub> +D Count | mean | SF        | %/PE   | N <sub>2</sub> Count | mean | %         | %/PE    |
|------|-------------------------|------|-----------|--------|----------------------|------|-----------|---------|
| 186f | 0.1.1.                  | 0.67 | 0.000017  | 0.001  | 6.3.2                | 3.7  | 0.0000917 | 0.0002  |
| 126f | 1.3.0                   | 1.3  | 0.00007   | 0.0076 | 14.8.8               | 10   | 0.0005    | 0.00098 |
| 66f  | 6.19.11                 | 12   | 0.0024    | 0.027  | 30.53.33             | 33.7 | 0.0077    | 0.015   |
| 0    | 9.26.17                 | 17.3 | 0.09 (PE) |        | 102.81.123           | 102  | 0.51 (PE) |         |

D<sub>2</sub>+D Count

|     |   |                |       |           |        |
|-----|---|----------------|-------|-----------|--------|
| 86f | 0 | 21. 17. 15     | 17.7  | 0.0004    | 0.0007 |
| 60f | 0 | 107. 114. 118  | 113   | 0.0113    | 0.018  |
| 46f | 0 | 159. 192. 189  | 180   | 0.09      | 0.163  |
| 0   | 0 | 147. 157. 128. | 126.3 | 0.63 (PE) |        |

No H<sub>2</sub>

TITLE:

DRUG: Taxol and TM 24 hrs prior X-ray

Investigator:

TUMOR: HTGBj, lateral cervical tumor size is 9 mm

P:1

Date:

Tumor size in mm

| group            | drug dose | radiation dose | #   | 0   | 1      | 2       | 3    | 4    | 5    | 6    | 7    | 8    | 9    | 10   | 11   |      |
|------------------|-----------|----------------|-----|-----|--------|---------|------|------|------|------|------|------|------|------|------|------|
| Control          | 100 mg/kg | 0.053          | 15  | 1   | 9 mm   | 10.5 mm | 10   | 9    | 8.5  | 8.0  | 7.5  | 8.0  | 7.5  | 8.0  | 8.0  | 7.0  |
|                  |           | 0.053          | 16  | 2   | 9 mm   | 10 mm   | 9    | 9.5  | 9    | 7.5  | 7.5  | 7.5  | 7.5  | 7.5  | 7.5  | 7.5  |
|                  |           | 0.053          | 16  | 3   | 9 mm   | 10.5 mm | 10.5 | 10   | 9.5  | 9.5  | 9.0  | 9.0  | 9.0  | 9.0  | 9.5  |      |
| 22 Gy            | 100 mg/kg | 0.053          | 15  | 4   | 9 mm   | 10.5 mm | 9    | 9    | 8    | 8.5  | 8.0  | 7.5  | 7.5  | 7.5  | 7.5  | 7.5  |
|                  |           | 0.053          | 15  | 2   | 9 mm   | 10 mm   | 9.5  | 9    | 8.5  | 8.0  | 8.0  | 8.0  | 7.5  | 7.5  | 7.5  | 7.5  |
|                  |           | 0.053          | 17  | 3   | 9 mm   | 10 mm   | 9    | 8.5  | 8    | 8.0  | 8.0  | 7.5  | 7.5  | 7.5  | 7.5  | 7.5  |
| 22 Gy Control RT |           | 0.053          | 15  | 1   | 9 mm   | 10 mm   | 11   | 11   | 11.5 | 11.0 | 12.0 | 12.0 | 13.0 | 14.0 | 15.0 |      |
|                  |           | 0.053          | 15  | 2   | 9      | 10      | 10   | 10   | 9.5  | 10.5 | 10.0 | 10.0 | 11.0 | 12.0 | 12.5 |      |
|                  |           | 0.053          | 15  | 3   | 9      | 9.5     | 10   | 10.5 | 10.0 | 10.5 | 9.5  | 9.5  | 9.5  | 10   | 11   |      |
|                  |           | 0.053          | 15  | 4   | 9      | 9.5     | 9.5  | 10   | 10.0 | 10.5 | 10.5 | 11.0 | 13.0 | 13.0 | 13.0 |      |
|                  |           | 0.053          | 15  | 5   | 9      | 9.5     | 10   | 10   | 10.5 | 11.5 | 11.0 | 12   | 13.0 | 14.0 | 15.0 |      |
|                  |           | 0.053          | 15  | 6   | 9      | 9.5     | 9.5  | 10.5 | 11.0 | 12   | 12   | 13.0 | 14.0 | 15.0 |      |      |
| TM Control       | 100 mg/kg | 0.053          | 16  | 4   | 7.5 mm | 9       | 4.5  | 9    | 8.5  | 7.5  | 7.5  | 7.0  | 7.0  | 7.5  | 7.5  |      |
|                  |           | 0.053          | 16  | 5   | 7.5 mm | 9       | 9.5  | 8.5  | 8    | 7.0  | 6.5  | 6.5  | 6.5  | 6.0  | 6.0  | dead |
|                  |           | 0.053          | 16  | 6   | 7.5 mm | 9       | 9.5  | 8.5  | 8    | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  |      |
| TM + 22 Gy       | 100 mg/kg | 0.053          | 17  | 4   | 9      | 9.5     | 9.5  | 9    | 9.0  | 8.5  | 8.5  | 8.5  | 8.5  | 8.5  | 8.5  |      |
|                  |           | 0.053          | 16  | 5   | 9      | 9.5     | 9.5  | 9.0  | 8.0  | 8.0  | 7.5  | 7.0  | 7.0  | 7.0  | 7.0  |      |
|                  |           | 0.053          | 18  | 6   | 9      | 9       | 9.5  | 8    | 7.5  | 7.5  | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  |      |
| Taxol + 22 Gy    |           | 0.062          | 18  | 1   | 9      | 9       | 8.5  | 8    | 8.0  | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  |      |
|                  |           | 0.053          | 16  | 2   | 9      | 10 RT   | 10   | 11   | 11.0 | 11.5 | 12.0 | 13   | 14.0 | 14.0 | 14.0 |      |
|                  |           | 0.053          | 16  | 3   | 9      | 10.5    | 10   | dead |      |
|                  |           | 0.053          | 16  | 4   | 9      | 10.5    | 9.5  | 9    | 8.5  | 8.0  | 7.5  | 7.0  | 7.0  | 7.0  | dead |      |
|                  |           | 0.053          | 17  | 5   | 9      | 10      | 7.0  | 7.5  | 8.0  | 8.0  | 7.0  | 6.5  | 6.5  | 6.5  | dead |      |
|                  |           | 0.053          | 16  | 6   | 9      | 9.5     | 8.5  | 8    | 8.0  | 7.5  | 6.5  | 6.5  | 6.5  | 6.5  | dead |      |
| Taxol Control    | 100 mg/kg | 0.053          | 17  | 1   | 9      | 9       | 8.5  | 8    | 8.0  | 7.5  | 7.0  | 6.5  | 6.5  | 6.5  | 6.5  | dead |
|                  |           | 0.053          | 15  | 2   | 9      | 8.5     | 8    | 7.5  | 7.5  | 7.5  | 7.0  | 6.5  | 6.5  | 6.5  | 6.5  | dead |
|                  |           | 0.053          | 15  | 3   | 9      | 9       | 8    | 8    | 7.5  | 7.0  | 7.0  | 6.5  | 6.5  | 6.5  | 6.5  | dead |
| Taxol Control    |           | 0.053          | 15  | 4   | 8      | 9       | 9    | 9    | 9.0  | 8.5  | 8.0  | 7.5  | 7.5  | 7.5  | 7.5  | dead |
|                  |           | 0.053          | 16  | 5   | 8      | 9       | 9    | 8.5  | 8.5  | 8.5  | 7.5  | 7.0  | 7.0  | 7.0  | 7.0  | dead |
|                  |           | 0.053          | 16  | 6   | 8      | 9       | 8    | 8    | 7.5  | 7.0  | 6.5  | 6.5  | 6.5  | 6.5  | 6.5  | dead |
| Control          |           | 1              | 8   | 8.5 | 9      | 9       | 10.0 | 11.0 | 12.0 | 12.5 | 13.5 | 14   | 14   | 14   | 14   | 14   |
|                  |           | 2              | 7   | 8   | 9      | 10      | 12.0 | 12.0 | 13.0 | 14   | 15   | 15   | 15   | 15   | 15   | 15   |
|                  |           | 3              | 8   | 7.5 | 9.5    | 10      | 11.5 | 12.0 | 13.5 | 14   | 14   | 14   | 14   | 14   | 14   | 14   |
|                  |           | 4              | 6   | 8   | 9      | 10      | 11.0 | 12.5 | 13   | 13   | 14   | 14   | 14   | 14   | 14   | 14   |
|                  |           | 5              | 7.5 | 9   | 11     | 11      | 12.0 | 13.0 | 14   | 14   | 15   | 15   | 15   | 15   | 15   | 15   |
|                  |           | 6              | 6.5 | 7.5 | 8.0    | 10      | 11.0 | 12.5 | 13.5 | 14.5 | 15   | 15   | 15   | 15   | 15   | 15   |
| Taxol            |           | 1              |     |     |        |         |      |      |      |      |      |      |      |      |      |      |
|                  |           | 2              |     |     |        |         |      |      |      |      |      |      |      |      |      |      |
|                  |           | 3              |     |     |        |         |      |      |      |      |      |      |      |      |      |      |

Tumor size in mm

dead

- 111. LE:

## DRUGS

Investigator :

P:2

10:39

ST. MARY'S MEDICAL CENTER

415 750 6215 P.06

- 111, LE :

DRUG :

Investigator :

P:3

ZUG:

estigator: p:4

Date: \_\_\_\_\_

Tumor size in mm

DRUG :

-TM drug

Investigator:

P. 1

Date: [REDACTED] Tumor size in mm

۱۶۵

UG :

### Stigator.

Tom drug

Date : 1

10. ~~10~~ Tumor size in mm

10:40

MARY'S MEDICAL CENTER

415 750 6215 P.08

DRUG : TM drug

vestigator: P:3

Date: [REDACTED] Tumor size in mm



| TNB   |  | Drug | X-ray | M | MOUSE 2 XLS |      |      |      |      |      |      |
|-------|--|------|-------|---|-------------|------|------|------|------|------|------|
| Group |  |      |       |   | 1           | 2    | 3    | 4    | 5    | 6    | 7    |
|       |  | B    |       |   | 1 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 2 8.5       | 10.0 | 11.0 | 12.5 | 14.0 | 14.5 | 15.0 |
|       |  |      |       |   | 3 15.0      | 15.5 | 16.0 | 17.0 | 18.0 | 18.5 | 19.0 |
|       |  |      |       |   | 4 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 5 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 6 16.5      | 16.5 | 16.5 | 16.5 | 17.0 | 17.0 | 17.0 |
|       |  | A    |       |   | 1 6.5       | 6.5  | 6.5  | 6.5  | 6.5  | 6.5  | 6.5  |
|       |  |      |       |   | 2 7.0       | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  | 7.0  |
|       |  |      |       |   | 3 8.0       | 8.0  | 8.0  | 8.0  | 8.0  | 8.0  | 8.0  |
|       |  |      |       |   | 4 8.5       | 8.5  | 8.5  | 8.5  | 8.5  | 8.5  | 8.5  |
|       |  |      |       |   | 5 9.0       | 9.0  | 9.0  | 9.0  | 9.0  | 9.0  | 9.0  |
|       |  |      |       |   | 6 9.5       | 9.5  | 9.5  | 9.5  | 9.5  | 9.5  | 9.5  |
|       |  | B    |       |   | 1 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 2 X         | X    | X    | X    | X    | X    | X    |
|       |  |      |       |   | 3 X         | X    | X    | X    | X    | X    | X    |
|       |  |      |       |   | 4 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 5 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 6 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  | A    |       |   | 1 8.5       | 8.5  | 10.0 | 10.5 | 11.0 | 12.0 | 12.0 |
|       |  |      |       |   | 2 X         | X    | X    | X    | X    | X    | X    |
|       |  |      |       |   | 3 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 4 X         | X    | X    | X    | X    | X    | X    |
|       |  |      |       |   | 5 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 6 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  | B    |       |   | 1 10.0      | 11.0 | 12.0 | 13.0 | 14.0 | 15.0 | 16.0 |
|       |  |      |       |   | 2 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 3 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 4 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 5 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 6 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  | A    |       |   | 1 12.5      | 13.0 | 13.5 | 14.0 | 14.5 | 15.0 | 15.5 |
|       |  |      |       |   | 2 8.0       | 8.0  | 8.0  | 8.0  | 8.0  | 8.0  | 8.0  |
|       |  |      |       |   | 3 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 4 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 5 0         | 0    | 0    | 0    | 0    | 0    | 0    |
|       |  |      |       |   | 6 0         | 0    | 0    | 0    | 0    | 0    | 0    |

TNTB

MOUSE2.xls

Tumor RT  
TNTB

| Group | Drug    | X-ray | M    | 1 | 2   | 3   | 4    | 5    | 6    | 7    | 8    | 9    | 10   | 11   | 12   | 13   | 14   | 15   | 16   | 17   | 18   | 19   | 20   | 21   | 22   | 23   | 24   | 25   | 26   |
|-------|---------|-------|------|---|-----|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| A     | Tumor   | RT    | 226f | 3 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | RT+TNTB | TNTB  | 226f | 6 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| B     | Tumor   | RT    | 10   | 4 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | TNTB    | RT    | 5    | 0 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| A     | Tumor   | RT    | 226f | 3 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | RT+TNTB | TNTB  | No   | 5 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| A     | Tumor   | RT    | 226f | 3 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | RT+TNTB | TNTB  | No   | 6 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| B     | Tumor   | RT    | 4    | 0 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | TNTB    | RT    | 5    | 0 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| A     | Tumor   | RT    | 226f | 3 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | RT+TNTB | TNTB  | No   | 6 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| B     | Tumor   | RT    | 10   | 4 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | TNTB    | RT    | 5    | 0 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| A     | Tumor   | RT    | 226f | 3 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|       | RT+TNTB | TNTB  | No   | 6 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| B     | Tumor   | RT    | 10   | 4 | 1.0 | 1.5 | 10.5 | 11.0 | 11.5 | 12.5 | 13.5 | 14.0 | 14.5 | 15.0 | 15.5 | 16.0 | 16.5 | 17.0 | 17.5 | 18.0 | 18.5 | 19.0 | 19.5 | 20.0 | 20.5 | 21.0 | 21.5 | 22.0 | 22.5 |
|       | TNTB    | RT    | 5    | 0 | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

TITLE :  
DRUG :

Investigator: TNB + 226g

Date:

TITLE :  
DRUG :

Investigator: TNB Control Date: [REDACTED]

.31  
3037.64

.21  
3053.64

| Group | Dose | 111      | 141          | 141<br>Diameter | Volume<br>Ratio | 151      | Volume<br>Ratio | Volume<br>mean | SD | SE | Ratio<br>mean | SD | SE |
|-------|------|----------|--------------|-----------------|-----------------|----------|-----------------|----------------|----|----|---------------|----|----|
|       |      | Diameter | Volume Ratio |                 |                 | Diameter |                 |                |    |    |               |    |    |
|       | 57   | 4.0      | 33.51        | 0.13            | 0               |          | 0               |                |    |    |               |    |    |
|       | 58   | 5.0      | 65.45        | 0.24            | 0               |          | 0               |                |    |    |               |    |    |
|       | 59   | 6.0      | 113.10       | 0.42            | 0               |          | 0               |                |    |    |               |    |    |
|       | 60   | 6.0      | 113.10       | 0.92            | 0               |          | 0               |                |    |    |               |    |    |
|       | 61   | 6.5      | 145.79       | 0.54            | 0               |          | 0               |                |    |    |               |    |    |
|       | 62   | 7.5      | 220.89       | 0.84            | 0               |          | 0               |                |    |    |               |    |    |
|       | 63   | 8.5      | 321.50       | 1.20            | 0               |          | 0               |                |    |    |               |    |    |
|       | 64   | 9.5      | 448.92       | 1.67            | 0               |          | 0               |                |    |    |               |    |    |
|       | 65   | 10.0     | 523.69       | 1.95            | 0               |          | 0               |                |    |    |               |    |    |
|       | 66   | 10.0     | 523.69       | 1.95            | 0               |          | 0               |                |    |    |               |    |    |
|       | 67   | 11.5     | 786.33       | 2.97            | 0               |          | 0               |                |    |    |               |    |    |
|       | 68   | 13.0     | 1150.35      | 4.29            | 0               |          | 0               |                |    |    |               |    |    |
|       | 69   | 14.0     | 1136.76      | 5.36            | 0               |          | 0               |                |    |    |               |    |    |
|       | 70   | 15.0     | 1767.15      | 6.59            | 0               |          | 0               |                |    |    |               |    |    |
|       | 71   | 16.5     | 2352.9       | 8.77            | 0               |          | 0               |                |    |    |               |    |    |
|       | 72   | 16.0     | 3053.64      | 11.39           | 0               |          | 0               |                |    |    |               |    |    |
|       | 132  |          |              | 0.0             | 14.14           |          | 0               |                |    |    |               |    |    |
|       | 133  |          |              | 4.0             | 33.51           |          | 0               |                |    |    |               |    |    |
|       | 134  |          |              | 5.0             | 65.45           |          | 0               |                |    |    |               |    |    |
|       | 135  |          |              | 6.0             | 113.10          |          | 0               |                |    |    |               |    |    |
|       | 136  |          |              | 7.0             | 179.59          |          | 0               |                |    |    |               |    |    |
|       | 137  |          |              | 7.5             | 220.89          |          | 0               |                |    |    |               |    |    |
|       | 138  |          |              | 8.0             | 265.8           |          | 0               |                |    |    |               |    |    |
|       | 139  |          |              | 8.5             | 321.50          |          | 0               |                |    |    |               |    |    |
|       | 140  |          |              | 9.0             | 321.50          |          | 0               |                |    |    |               |    |    |
|       | 141  |          |              | 9.0             | 381.70          |          | 0               |                |    |    |               |    |    |
|       | 142  |          |              | 9.5             | 448.92          |          | 0               |                |    |    |               |    |    |
|       | 143  |          |              | 10.0            | 523.69          |          | 0               |                |    |    |               |    |    |
|       | 144  |          |              | 10.5            | 606.13          |          | 0               |                |    |    |               |    |    |
|       | 145  |          |              | 10.5            | 606.13          |          | 0               |                |    |    |               |    |    |
|       | 146  |          |              | 11.0            | 646.91          |          | 0               |                |    |    |               |    |    |
|       | 147  |          |              | 11.5            | 786.33          |          | 0               |                |    |    |               |    |    |
|       | 148  |          |              | 12.5            | 1022.66         |          | 0               |                |    |    |               |    |    |
|       | 149  |          |              | 13.0            | 1150.35         |          | 0               |                |    |    |               |    |    |
|       | 150  |          |              | 13.0            | 150.35          |          | 0               |                |    |    |               |    |    |
|       | 151  |          |              | 13.5            | 1288.35         |          | 0               |                |    |    |               |    |    |
|       | 152  |          |              | 14.0            | 1436.76         |          | 0               |                |    |    |               |    |    |
|       | 153  |          |              | 14.5            | 158.35          |          | 0               |                |    |    |               |    |    |
|       | 154  |          |              | 15.0            | 1767.15         |          | 0               |                |    |    |               |    |    |
|       | 155  |          |              | 16.0            | 2449.67         |          | 0               |                |    |    |               |    |    |
|       | 156  |          |              | 17.0            | 321.50          |          | 0               |                |    |    |               |    |    |
|       |      |          |              | 18.0            | 383.64          |          | 0               |                |    |    |               |    |    |